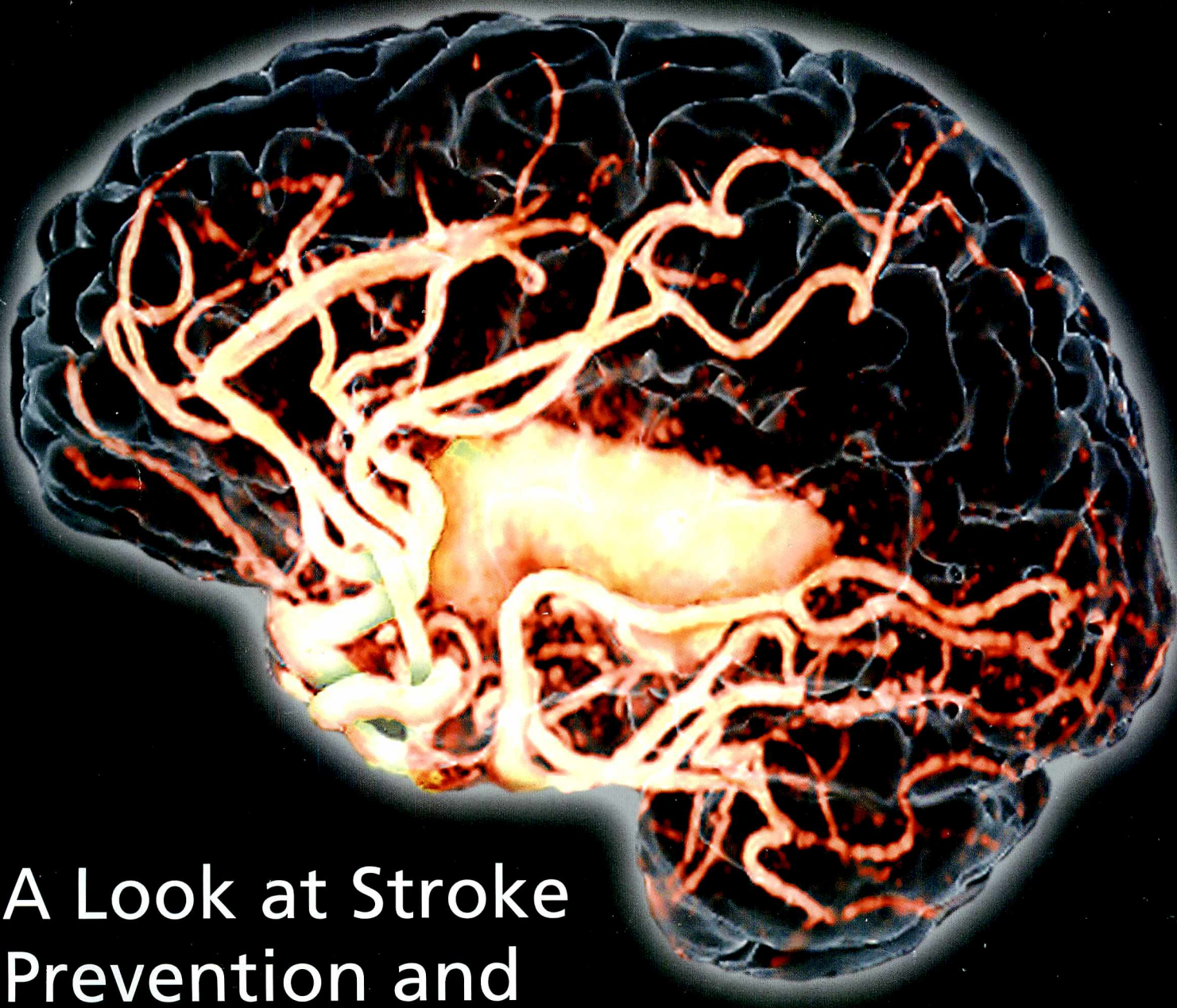


FDA *Consumer*

The Magazine of the U.S. Food and Drug Administration

March–April 2005 • Vol. 39 No. 2

Brain Attack



A Look at Stroke
Prevention and
Treatment



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FDA Consumer

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OBSERVATIONS

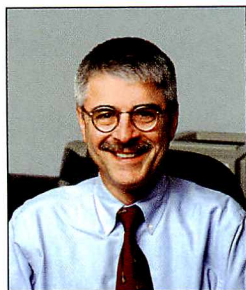
Stroke is the third-leading cause of death and the leading cause of long-term disability in the United States. About 500,000 new strokes and about 160,000 stroke-related deaths are reported each year, according to the National Institute of Neurological Disorders and Stroke (NINDS).

Strokes occur when the blood flow to the brain is interrupted by either a blockage or rupture of a blood vessel or artery. A stroke caused by a blood clot that keeps blood from reaching the brain is called an ischemic stroke. A stroke that occurs when a blood vessel in the brain ruptures is called a hemorrhagic stroke. About 8 out of 10 strokes reported in the United States annually are ischemic strokes.

Also called a brain attack, stroke often comes on suddenly. However, the conditions that make a stroke more likely often take years to develop. According to the NINDS, the best treatment for stroke is prevention. High blood pressure, heart disease, smoking, diabetes, and high cholesterol are among the risk factors that increase the likelihood of stroke. Experts say that people who quit smoking and who keep their blood pressure, cholesterol, and diabetes under control significantly reduce their chances of having a stroke.

Find out more about stroke, how to reduce the risk of having one, and the latest on treatments, in our cover story titled "Brain Attack," beginning on page 20.

Nerve impulses travel throughout our bodies along nerve cells called neurons. Nerve fibers called axons may link to



other neurons or other cells. Some nerve fibers have a fatty coating on them that helps speed up the transmission of nerve impulses. This coating is called the myelin sheath.

In people who have multiple sclerosis (MS), small areas of this protective sheath are damaged. Once the myelin sheath is damaged, nerve impulses cannot be conducted normally and communication between the brain and muscle breaks down, according to the NINDS.

Doctors still don't know what causes MS. But a new treatment recently approved by the FDA holds promise for the future. For more on MS, see our feature article titled "New Treatment, New Hope for Those With Multiple Sclerosis," beginning on page 10.

Used literally, the word arthritis means inflammation of the body's joints. As it's usually used, the word refers to a group of more than 100 rheumatic diseases that cause joint swelling, stiffness, and pain, according to the National Institute of Arthritis and Musculoskeletal and Skin Diseases. However, the diseases also can affect other muscles, bones, tendons, and even some internal organs. For an update on arthritis treatments and the latest on how to minimize the impact of the condition on your lifestyle, see "Helpful Treatments Keep People With Arthritis Moving," beginning on page 30.

We also take a look at the latest revision of the federal government's dietary guidelines, the potential hazards of tanning devices, and at a new tool that doctors are using to examine the digestive tract.

Raymond Formanek Jr.
Editor

UPDATES

First-of-a-Kind Genetic Lab Test

The FDA has cleared for marketing the first laboratory test system that will allow physicians to consider unique genetic information in selecting medications and doses of medications for a variety of common conditions, including heart disease, psychiatric disease, and cancer.

"Physicians can use the genetic information from this test to prevent harmful drug interactions and to assure drugs are used optimally, which in some cases will enable patients to avoid less effective or potentially harmful treatment choices," says Acting FDA Commissioner Dr. Lester M. Crawford.

Manufactured by Roche Molecular

Systems Inc. of Pleasanton, Calif., the AmpliChip Cytochrome P450 Genotyping Test is the first DNA microarray test to be cleared by the FDA. A microarray is similar to a computer microchip, but instead of tiny circuits, the chip contains millions of tiny DNA molecules. The test is performed using DNA that is extracted from a patient's blood.

The new test analyzes one of the genes from a family of genes called cytochrome P450. The enzymes produced from these genes are active in the liver to break down certain drugs and other compounds. Variations in this family of genes can cause a patient to metabolize certain drugs more

quickly or more slowly than average, or, in some cases, not at all. The specific gene that is analyzed by this test plays an important role in the body's ability to metabolize some commonly prescribed drugs, including antidepressants, antipsychotics, beta blockers, and some chemotherapy drugs.

Cleared for use with the Affymetrix GeneChip Microarray Instrumentation System manufactured by Affymetrix Inc. of Santa Clara, Calif., the test is not intended to be used by itself to determine the optimum drug dosage. The test should be used along with clinical evaluation and other tools to determine the best treatment options for patients.

New Warning for ADHD Drug

Labels for Strattera (atomoxetine) will now carry a bolded warning about the potential for severe liver injury. Strattera is a drug approved by the FDA for attention-deficit hyperactivity disorder (ADHD) in adults and children. The labeling update follows the reports of severe liver injury in one teen-ager and one adult, both of whom recovered, who had been treated with Strattera for several months.

The labeling warns that severe liver injury may progress to liver failure resulting in death or the need for a liver transplant in a small percentage of people who take Strattera.

The warning also indicates that the medication should be discontinued in people who develop a yellowing of the skin or whites of the eyes (jaundice) or laboratory evidence of liver injury.

Strattera has been on the market since 2002 and has been used in more than 2 million people. In clinical trials involving 6,000 patients, no signal of liver problems (hepatotoxicity) had emerged.

The FDA has asked the manufacturer, Eli Lilly and Company of Indianapolis, to add the bolded warning about severe liver injury to the labeling. Eli Lilly has agreed to alert health care professionals about the new information in a "Dear Health Care Professional" letter. The company will also update the patient package insert with information about the signs and symptoms of liver problems, which include itchy skin, jaundice, dark urine, upper right-sided abdominal tenderness, and unexplained "flu-like" symptoms.

New Drug to Treat Cancer-Related Mouth Sores

Painful sores and ulcers in the lining of the mouth are a common complication of the high-dose chemotherapy and radiation therapy regimens associated with bone marrow transplants. Patients suffering from the complication, called mucositis, have difficulty eating and swallowing. In the most

severe form of mucositis, patients cannot eat or drink at all and must receive nutrition and fluid replacement through their veins.

The FDA has approved a treatment called Kevivance (palifermin) to help prevent mucositis. The drug also shortens the duration of the condition.

Kevivance is a synthetic version of a naturally occurring human protein called keratinocyte growth factor (KGF) that stimulates the growth of cells in the skin and on the surface layer of the mouth, stomach, and colon. Kevivance, like the natural KGF, also stimulates cells on the surface layer of the mouth to grow. This is thought to lead to faster replacement of these cells when killed by the cancer treatments and is believed to speed up the healing process of mouth ulcers.

Kevivance, which has been shown to be safe and effective only in those being treated for leukemia and lymphoma, is manufactured by Amgen Inc. of Thousand Oaks, Calif.

Warning on Imported Ginseng

The FDA has issued a warning to people who may have used imported ginseng from FCC Products Inc., based in Livingston, N.J. The ginseng products are considered adulterated under the Federal Food, Drug, and Cosmetic Act because they contain



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unsafe chemical residues from the pesticides procymidone and quintozone.

These residues are deemed unsafe because there has been no maximum amount of residues allowed (tolerance) established for them in ginseng. The FDA is responsible for enforcing pesticide tolerances and food additive regulations. A raw agricultural commodity or processed food or feed is deemed to be unsafe and adulterated if a pesticide

chemical residue for which no tolerance has been set is present.

At the FDA's request, the U.S. District Court for the District of New Jersey issued a warrant for the seizure of these products. The U.S. Marshals Service, accompanied by an FDA investigator, seized the ginseng in December 2004.

'Black Box' Warning Added to Contraceptive Injection

The physicians' labeling of Depo-Provera Contraceptive Injection will now carry a "black box" warning to highlight that prolonged use of the drug may result in loss of bone density. The FDA has approved the injectable drug for use in women to prevent pregnancy.

Depo-Provera Contraceptive Injection has been used for decades for birth control throughout the world and it remains a safe and effective contraceptive. The FDA and New York City-based Pfizer Inc., the drug's manufacturer, are issuing the warning to ensure that patients and physicians have access to the important information.

The loss of bone density is greater the longer the drug is taken, and this loss may not be completely reversible after discontinuing the drug. The warning states that a woman should only use Depo-Provera Contraceptive Injection as a long-term birth control method, for example, longer than two years, if other birth control methods are inadequate.

Black box warnings are designed to highlight special or serious problems about an FDA-regulated product. The warnings help physicians to prescribe a drug that may be associated with serious side effects in a way that maximizes its benefits and minimizes its risks.

The warning is based on analyses by Pfizer and the FDA of data that clarified the drug's long-term effects on bone density.

The company will incorporate the new information in the patient information sheet distributed with the drug.

Clinical Trial of Iressa

In December 2004, the FDA learned from AstraZeneca Pharmaceuticals that a large clinical trial comparing Iressa (gefitinib) with an inactive substance (placebo) showed no survival benefit from taking Iressa. The study involved people with non-small cell lung cancer who had failed other courses of cancer therapy.

People who take Iressa should consult their physicians as soon as possible, but they should not change their therapy without first talking to a health care professional.

Alternative therapies are available. The FDA has approved Taxotere (docetaxel) and Tarceva (erlotinib), both of which have been shown in studies to improve survival in people with non-small cell lung cancer whose cancer has progressed while on previous therapies.

The FDA approved Iressa on May 2, 2003, under the agency's accelerated approval program. This program allows the agency to approve a drug for marketing based on how it affects a surrogate endpoint—such as a sign of a disease or the results of a laboratory test—that is considered reasonably likely to predict clinical benefit, such as improved symptoms or survival.

Iressa was approved because the data from clinical trials showed that it caused significant shrinkage in tumors in about 10 percent of patients, and this was thought likely to increase patients' overall survival time.

One requirement for drugs approved under accelerated approval is that the sponsor must study them further to verify the expected clinical benefit. After the approval of Iressa, AstraZeneca, based in Wilmington, Del., conducted a study in about 1,700 patients to determine whether the drug would in fact prolong survival in comparison to patients taking a placebo. The results indicate that the drug did not prolong survival.

Under the FDA's accelerated approval program, the agency has the authority

to remove a drug from the market if a postmarketing clinical study fails to verify clinical benefit. After the FDA has evaluated the recent study results, the agency will determine whether Iressa should be withdrawn from the market or if other regulatory actions are appropriate.

New Drug Treats Age-Related Macular Degeneration

A new therapy to slow vision loss in people with wet age-related macular degeneration (AMD), an eye disease that destroys central vision, has been approved by the FDA.

Macugen (pegaptanib sodium injection) is the first in a new class of ophthalmic drugs to specifically target vascular endothelial growth factor (VEGF), a protein that acts as a signal in triggering the abnormal blood vessel growth and leakage that is the hallmark of wet AMD.

AMD is the leading cause of irreversible blindness in patients older than 50 in developed countries. According to a study in the April 2004 issue of *Archives of Ophthalmology*, AMD is the leading cause of blindness for white Americans, with 1.8 million cases reported in 2002.

The disease occurs in two forms: wet and dry. Wet AMD occurs when abnormal blood vessels behind the retina start to grow under the macula—located in the center of the retina. These new blood vessels tend to be fragile and often leak blood and fluid. The blood and fluid raise the macula from its normal place at the back of the eye, causing rapid damage to occur. An early symptom of wet AMD is straight lines that appear wavy.

Dry AMD occurs when the light-sensitive cells in the macula slowly break down, gradually blurring central vision

in the affected eye. The most common symptom of this type is slightly blurred vision. Wet AMD, which makes up about 10 percent of AMD cases, is considered to be more severe than the dry form.

Approved for marketing in December 2004, Macugen is a single strand of nucleic acid that specifically binds to a particular protein that plays a critical role in the formation of new blood vessels and increased leakage from blood vessels—two of the primary pathological processes responsible for the vision loss associated with wet AMD.

Macugen therapy was co-developed by Eyetech Pharmaceuticals Inc. and Pfizer Inc., both of New York City.

Canadian Company Recalls Bipolar Disorder Drug

The FDA is warning people not to buy or use Carbolith (lithium carbonate) 150-milligram capsules for treating bipolar disorder, also called manic-depressive illness, a serious psychiatric condition. Valeant Canada Ltd. of Montreal recalled the capsules after testing indicated that the product may not deliver adequate amounts of the drug to ensure effective treatment.

Health Canada recently advised people taking Carbolith 150 to continue taking their medicine and to consult with their health care professionals as soon as possible. Americans who have purchased the drug through the Internet and taken it for bipolar disorder could experience adverse events associated with lowered blood lithium levels, including a worsening of the illness.

In addition, people who may have taken the Carbolith product for several weeks or longer may experience toxic effects, such as confusion, muscle twitching, vomiting, and diarrhea, when they switch to a lithium carbonate product that delivers adequate amounts of the drug.

A public advisory issued by Health Canada about this recall can be found at www.hc-sc.gc.ca/english/protection/warnings/2004/2004-10-29.html.

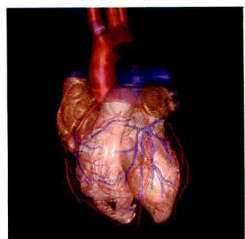


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FDA Warning on NSAID Use

The FDA issued a public health advisory in December 2004 concerning use of non-steroidal anti-inflammatory drugs (NSAIDs), including those known as COX-2 selective agents. The public health advisory is an interim measure, pending further review of data that continue to be collected.

Recently released data from controlled clinical studies showed that the COX-2 selective agents Vioxx (rofecoxib), Celebrex (celecoxib), and Bextra (valdecoxib) may be associated with an increased risk of serious cardiovascular events, such as heart attack and stroke, especially when used for long periods or in very high-risk settings, such as immediately after heart surgery.



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In addition, preliminary results from a long-term clinical trial—up to three years—suggest that long-term use of the non-selective NSAID Aleve (naproxen) may be associated with an increased cardiovascular risk compared to an inactive substance (placebo).

Specifically, the public health advisory recommends that

- Physicians prescribing Celebrex or Bextra should consider the emerging information when weighing the benefits against the risks for individual patients. Those at a high risk for gastrointestinal bleeding, who have a history of intolerance to non-selective NSAIDs, or who are not doing well on non-selective NSAIDs may be appropriate candidates for COX-2 selective agents. Vioxx was voluntarily withdrawn from the market by its manufacturer, Merck & Co. Inc., in late 2004.

- Individual patient risk for cardiovascular events and other risks commonly associated with NSAIDs should be taken into account for each prescribing situation.

- Consumers are advised that all over-the-counter (OTC) pain medications, including NSAIDs, should be used in strict accordance with the label directions. If use of an OTC NSAID is needed for longer than 10 days, a physician should be consulted.

The FDA will continue to analyze all available information from new studies of Vioxx, Celebrex, Bextra, and naproxen and other data for non-selective NSAIDs and COX-2 selective products to determine whether additional regulatory action is needed.

Final Rule Enhances Food Security

The FDA has issued a final record-keeping rule to protect the U.S. human food and animal feed supply in the event of serious health threats. Under the authority of the Bioterrorism Act of 2002, the regulation requires people who manufacture, process, pack, transport, distribute, receive, hold, or import food to establish and maintain records.

The records identify the immediate previous source of all food received, as well as the immediate subsequent recipient of all food released. Records must be retained at the establishment where the activities covered in the records occurred or at an accessible location. Food companies may keep the information in any format, paper or electronic. All businesses covered by the rule must comply within 12 months from Dec. 9, 2004, the date the rule was published in the *Federal Register*, except small businesses, which have 18 months to comply, and very small businesses, which have 24 months.

When the FDA has a reasonable belief that an article of food is adulterated and presents a serious threat to humans or animals, any records or other information to which the FDA has access must be available for inspection and copying as soon as possible, and no later than 24 hours from the time an official request is made.

The Bioterrorism Act allows the FDA to bring civil action in federal court to enjoin the people who fail to comply with this rule. The FDA can also seek criminal actions in federal court to prosecute those who fail to establish and maintain records as required by the rule. ■

We're eager to hear what you like and what you don't like. We also want to know the subjects you'd like to see covered.

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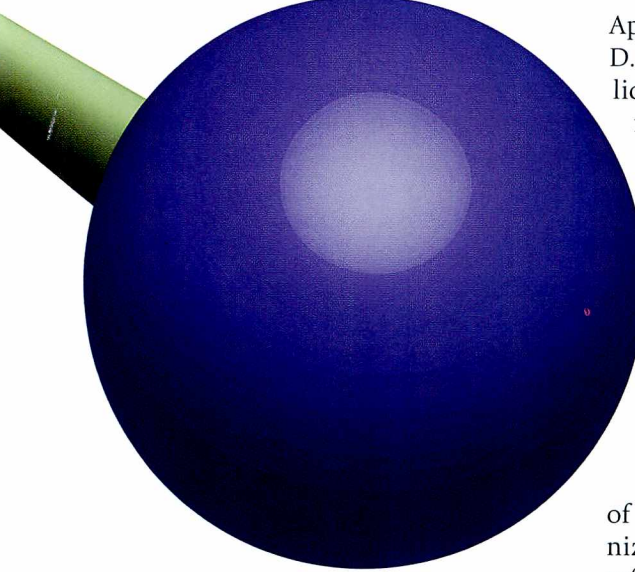


FDA Science Forum:

Advancing Public Health

By Michelle Meadows

You don't have to know the difference between a virus and a bacterium to benefit from the Food and Drug Administration's 2005 Science Forum, an annual event aimed at sharing the science behind the agency's regulatory decisions.



This year's forum is scheduled for April 27–28, 2005, at the Washington, D.C., Convention Center. A free public session targeted to consumers is set for April 26. FDA experts and other health professionals will conduct the "plain English" session.

With the theme "Advancing Public Health Through Innovative Science," this year's science forum will showcase the FDA's scientific achievements, encourage discussions on FDA topics, promote collaboration, and recognize outstanding research.

Lawrence X. Yu, Ph.D., chairman of the 2005 FDA Science Forum organizing committee, says, "'Advancing' reflects the FDA's mission to protect

and advance the public health and 'Innovative' reflects the FDA's good manufacturing practices and critical path initiatives." The FDA's critical path initiative centers on spurring the development of new medical products.

Sessions at the science forum will cover a range of topics, from emerging technologies for cancer diagnosis and treatment to advances in fighting contagious diseases and bioterrorism. Along with giving presentations, experts will also exhibit scientific posters.

Yu says this year's forum has several new features, including a session called "Meet the Center Directors" and interactive roundtable discussions with FDA leaders on clinical trials, immunology, toxicology, and other timely topics.

Meet the Center Directors

On April 28, participants of the 2005 FDA Science Forum will hear from the following directors of the Food and Drug Administration's product review and research centers on what issues they think will be of critical importance during the year.

- Jesse Goodman, M.D., M.P.H., Center for Biologics Evaluation and Research
- Daniel Schultz, M.D., Center for Devices and Radiological Health
- Steven K. Galson, M.D., M.P.H., Center for Drug Evaluation and Research
- Robert Brackett, Ph.D., Center for Food Safety and Applied Nutrition
- Stephen Sundlof, D.V.M., Ph.D., Center for Veterinary Medicine
- Daniel Casciano, Ph.D., National Center for Toxicological Research
- John M. Taylor, Esq., Office of Regulatory Affairs ■

For Consumers

The FDA remains committed to increasing consumer understanding of FDA issues. This is the second year that the science forum will offer a free public session. Titled "Personalizing Your Healthcare: The Best Consumer Is an Educated Consumer," the program will give consumers an opportunity to learn about personalized medicine, generic drugs, and nutrition. Janet Woodcock, M.D., acting deputy commissioner for operations at the FDA, will lead the session, scheduled for 1 p.m. to 5 p.m. on April 26.

Personalized medicine: Felix Frueh, Ph.D., a scientist with the FDA's Center for Drug Evaluation and Research, and Finley Austin, an expert at the Personalized Medicine Coalition in Washington, D.C., will discuss the growing role of personalized medicine in health care.

"We know that genetic variations can affect how individuals respond to disease and to drugs," Frueh says. Personalized medicine involves getting the best medical outcomes by choosing treatments that work well with a person's genetic profile, or with certain characteristics in the person's blood proteins or cell surface proteins.

For example, personalized medicine could include the use of a genetic test that can assess the likelihood that someone with breast cancer will have a recurrence. Another example is using genetic information to help health professionals select a type of medication or the dose.

Frueh cites the drug Tarceva (erlotinib) as a recent example of a drug with a label that shows how people

hler, R.Ph., director of the FDA's Office of Generic Drugs, will give presentations in a session titled, "Generic Drugs: Are They Really As Good?"

"Consumer confidence in generics is increasing," Buehler says. "More products are becoming available in generic form and consumers have grown to trust their quality." This session will provide an understanding of the FDA's review and approval process for generic drugs.

"We learn very early that cost usually goes hand in hand with quality," Buehler says. "But for generic drugs, the cost differential is linked to the requirements for approval, not quality or ingredients. Because manufacturers of generics don't have to perform the expensive efficacy and safety testing, generics can be made and sold less expensively. The FDA assures that the products are manufactured to meet the same rigid standards as the brand products, and that the generics are shown

director of the Office of Nutritional Products, Labeling, and Dietary Supplements, part of the FDA's Center for Food Safety and Applied Nutrition, is one of the presenters. "The session will discuss the dietary and lifestyle factors that are associated with improving health and reducing the risk of chronic disease," Schneeman says. Janet King, Ph.D., chairwoman of the Dietary Guidelines Advisory Committee, also will make a presentation.

Dietary guidelines are updated and released every five years and contain the latest nutritional and dietary guid-

... generics are less expensive than brand-name products, and they are also as safe and effective.

who seem the same can respond differently to treatments. The FDA approved Tarceva in November 2004 for certain people with lung cancer. Tarceva was developed to block an important signal that stimulates the growth of cancer cells.

Frueh says, "From a regulatory perspective, we want to package information about genetics in a way that is understandable for patients and physicians. A drug label needs to be scientifically sound, but it also needs to be possible for people without formal training in genetics to understand this additional information and its implications."

Generic drugs: Jack Billi, M.D., associate vice president at the University of Michigan, and Gary Bue-

hler, R.Ph., director of the FDA's Office of Generic Drugs, will give presentations in a session titled, "Generic Drugs: Are They Really As Good?"

The FDA is partnering with many pharmacies and insurance companies to get the message out that generics are less expensive than brand-name products, and they are also as safe and effective. "This is especially important because we know that many consumers have difficulty affording many of the prescription drugs they need," Buehler says.

Dietary guidelines and nutrition: A session focusing on the connection between food and health is titled, "Are You What You Eat? A Critical Look at the New Dietary Guidelines for Americans, the Science of Nutrition, and Personal Choices for a Healthier Life."

Barbara O. Schneeman, Ph.D.,

director of the Office of Nutritional Products, Labeling, and Dietary Supplements, part of the FDA's Center for Food Safety and Applied Nutrition, is one of the presenters. "The session will discuss the dietary and lifestyle factors that are associated with improving health and reducing the risk of chronic disease," Schneeman says. Janet King, Ph.D., chairwoman of the Dietary Guidelines Advisory Committee, also will make a presentation.

Dietary guidelines are updated and released every five years and contain the latest nutritional and dietary guidance for the general public. For example, the guidance stresses the health benefits of a diet that's low in saturated fat and cholesterol and high in fruits and vegetables.

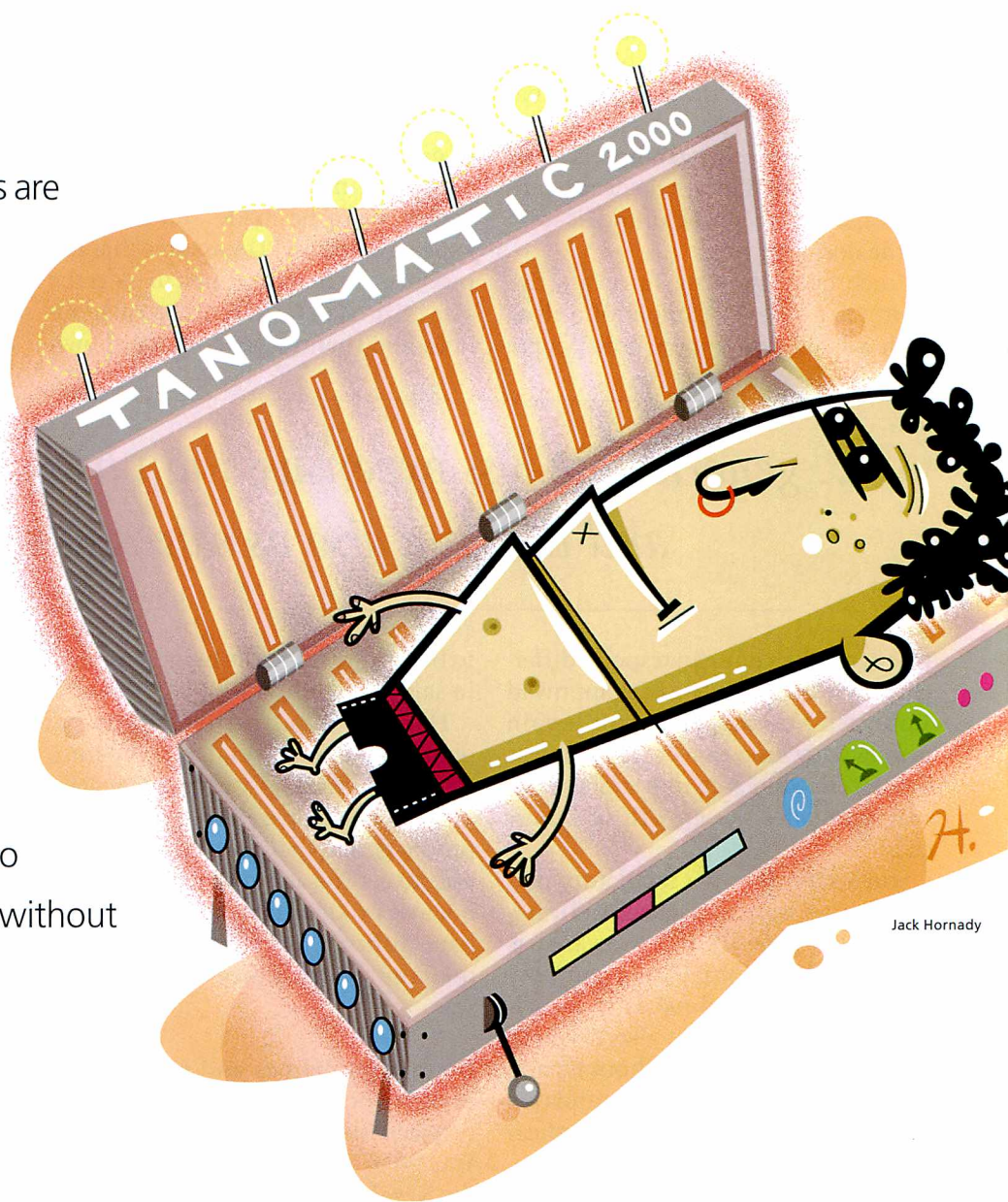
Schneeman says, "We want to help consumers understand the connection between scientific evidence and recommendations that the government will use to support its education and public health programs." The dietary guidelines establish the direction for government nutrition programs, including research, education, labeling, and nutrition promotion.

Registration for the free public session and the regular forum is required. Information is available at www.fda.gov/scienceforum. ■

Teen Tanning HAZARDS

By Carol Rados

Parents of teen-agers are strongly encouraged by public health experts and medical professionals to discuss with their kids the dangers of indoor tanning equipment, and even to discourage its use. In fact, legislators in some states are proposing to make it illegal for a teen to tan in a commercial salon without parental consent.



Jack Hornady

According to the American Cancer Society (ACS), exposure to the sun's ultraviolet (UV) rays appears to be the most important environmental factor in developing skin cancer. Consequently, the dangers from exposure to UV rays from artificial sources of light, such as tanning beds and sunlamps, are similar to the dangers of exposure to sunlight. Moreover, some experts

to protect people from acute burns and exposure to hazardous shortwave UV radiation that was unnecessary for tanning.

In 1985, the agency decided to amend the standards to make the requirements more compatible with then-current products. When sunlamp technology changed and sunlamps emitting primarily UVA radiation—longer-wave,

Cyr and Miller warn that, in practice, tanning salon operators control the exposure time and that they may allow the customer to exceed exposure times written on the label. This is especially true for the beginning of the tanning course when users are advised to start off with very short exposures, usually five minutes or less. Fox says that people who use these products should

'Just one sunburn increases your risk for skin cancer.'

strongly believe that the sharp rise in the rates of the most serious type of skin cancer—malignant melanoma—may be due to increased exposure to UV radiation, whether from natural sunlight or artificial sources of light.

When exposed to UV radiation, the skin begins to produce a pigment called melanin to protect itself from burning. It is the production of melanin that causes the skin to darken and produce the tan. The production of new melanin takes three to five days.

Joshua L. Fox, M.D., a dermatologist in Fresh Meadows, N.Y., says, "Continued use of a tanning bed or sunlamp can be quite dangerous, particularly during the teen-age years." Teens are at greater risk, he says, because they are still experiencing tremendous growth at the cellular level, and, like other cells in the body, the skin cells are dividing more rapidly than they do during adulthood.

W. Howard Cyr, Ph.D., and Sharon A. Miller, both laboratory leaders in the Food and Drug Administration's Center for Devices and Radiological Health, say that the agency has regulated the manufacture of sunlamp products—sunlamps, tanning beds, tanning booths, and other related equipment—since 1979. Initially, there was a widespread acute risk from sunlamp products, as indicated by a large number of skin and eye injuries treated annually in hospital emergency rooms. Federal performance standards for sunlamp products were established

less efficient at producing a sunburn—became prevalent, longer exposure times were allowed, Miller says.

In 1986, the FDA published a policy letter that described how the maximum timer limit should be determined and provided guidance on recommended exposure schedules. The manufacturers of sunlamp products are required to include a recommended exposure schedule in their labeling. This schedule should be clearly visible to users before they begin their exposure session.

"FDA does not recommend the use of indoor tanning equipment," Miller says. Fox agrees. "There is no such thing as a safe tan," he says. "Just one sunburn increases your risk for skin cancer."

However, Miller says that if people insist on using tanning devices, there are things they can do to reduce the potential dangers.

"Start slowly, with short exposure times, and build up to a tan. If you get the maximum exposure the first time, you will probably get burned," Miller says. And, she adds, often people don't even know they are burned until it's too late. "Remember that a sunburn doesn't usually show up until several hours after the exposure," she says. In addition, the recommended exposure schedules do not allow for tanning more frequently than every other day. After a tan is developed, tanning frequency should be reduced to no more than twice a week.

always ask to see the information contained in the label. Be wary, he adds, if tanning salon operators can't produce it.

Miller says that the use of FDA-compliant eyewear that blocks UV rays is absolutely essential for tanning bed users to protect their eyes from corneal burns and cataracts from long-term exposure.

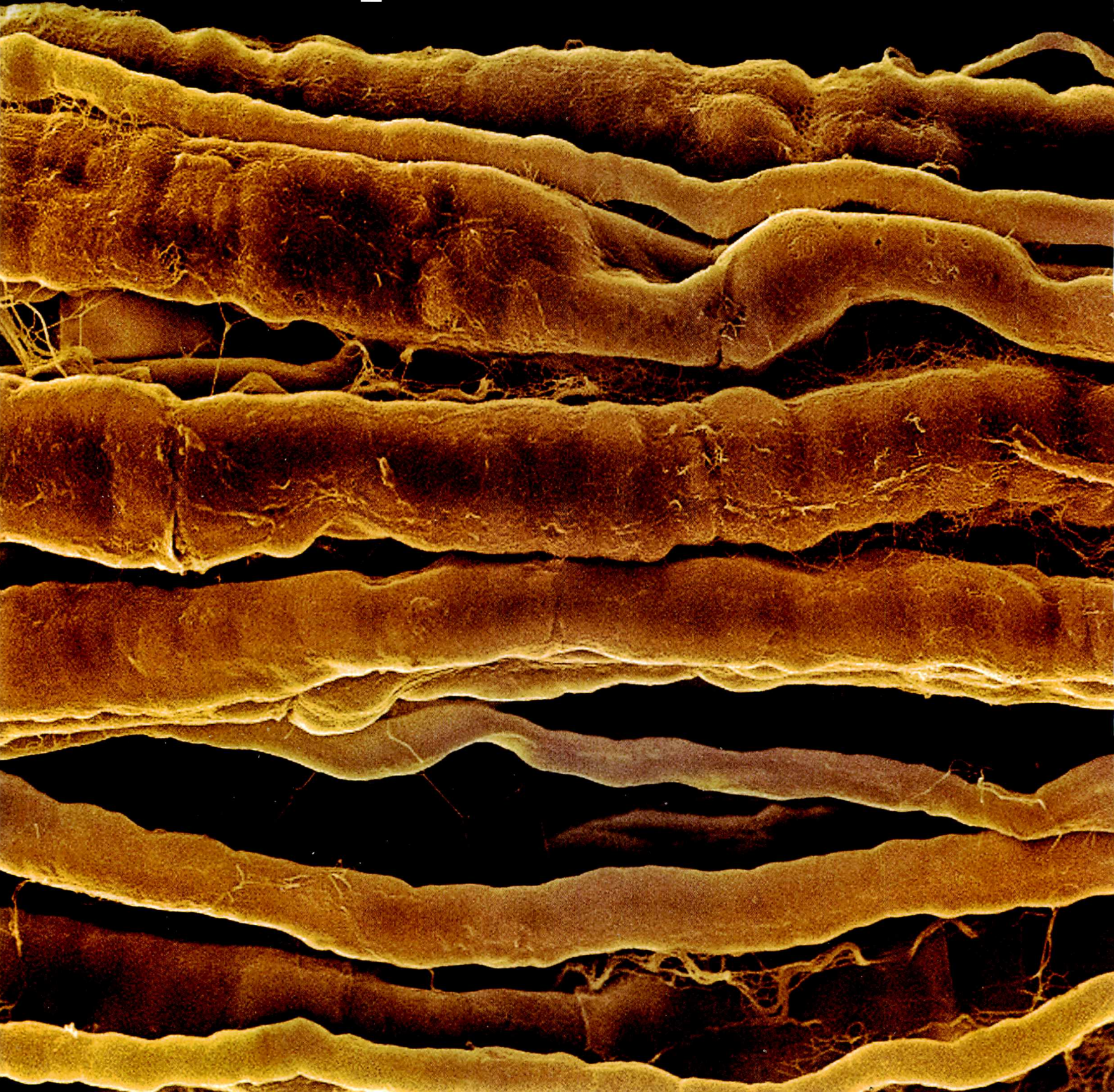
A study done by researchers at Wake Forest University, published in the July 2004 issue of the *Journal of the American Academy of Dermatology*, found that participants thought UV exposure was not only desirable for improving appearances, but also was somewhat addictive. The study concluded that "The relaxing and reinforcing effects of UV exposure contribute to tanning behavior in frequent tanners and should be explored in greater detail."

Fox advises parents to explore safer, alternative means for their children to acquire a tan. "Teens should know about the options," he says, which include self-tanners in the form of creams and gels. "Get the look you like without the damage that can occur with tanning equipment." ■

For More Information

FDA Q's and A's on tanning
www.fda.gov/cdrh/consumer/tanning.html

New Treatment, New Hope
for Those With
Multiple Sclerosis

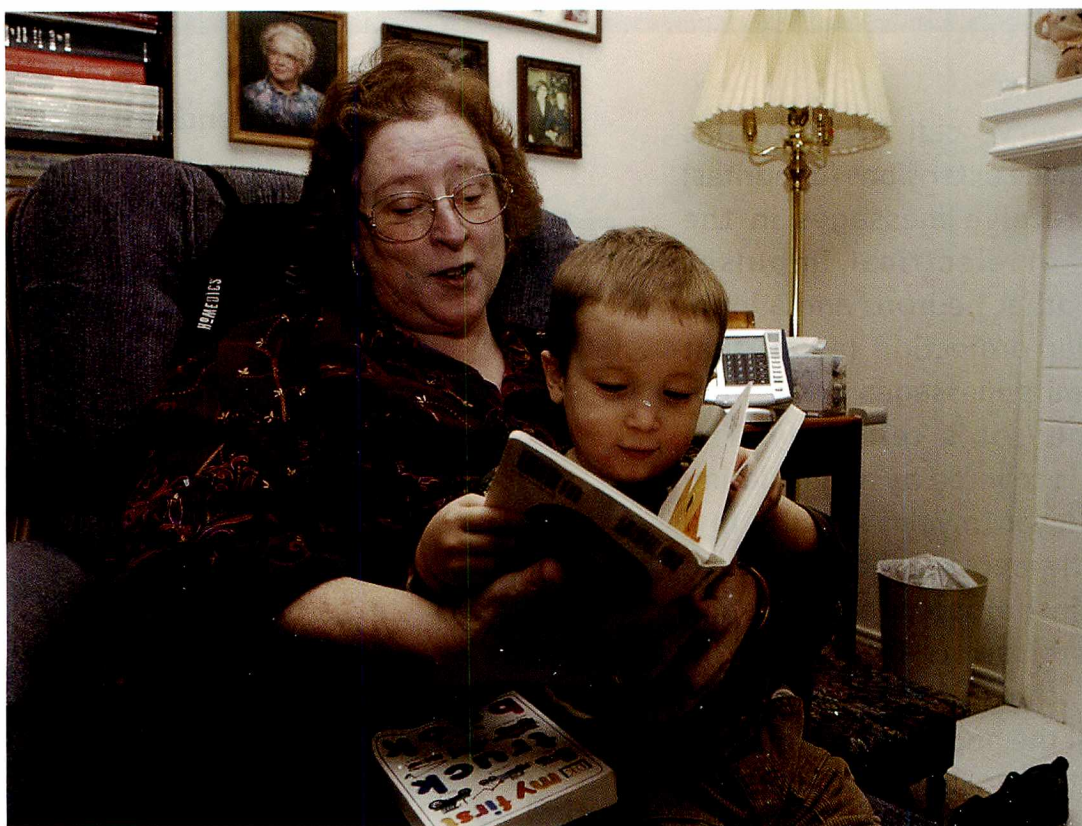


By Linda Bren

Shari Ferko feared the worst when she was diagnosed with multiple sclerosis in 1990. Her ability to walk was declining and she might soon need a cane and eventually a wheelchair, she thought. She wasn't even sure she'd be around to see her children grow up.

"It was a scary prospect," says the Dallas mother of two, whose children were 7 and 8 at the time. "I thought, 'These kids need their Mom. Will I even see them graduate from high school?'"

But Ferko did see her children graduate, and today, at age 48, she chases after a grandchild when she isn't working at a desk three days a week as a nurse. "I'm still not using a cane and I only use a wheelchair for long distances," says Ferko, who didn't let her disease keep her from touring Europe last year.



Biogen Idec Inc.

Shari Ferko spends time with her grandson, Alex. Ferko says she does everything at a slower pace than most people because of her multiple sclerosis.

A photo of nerve fibers taken through a microscope.

Photo Researchers Inc.

'It's a disease that strikes people typically in the prime of their life.'

Ferko takes medications to help relieve fatigue, spasms, blurred vision, and bowel and bladder problems, all common symptoms of multiple sclerosis (MS). And she is now taking the latest drug to treat MS approved by the Food and Drug Administration. She knows there is no cure for the disease that attacks the central nervous system, but she's hoping that the new treatment will keep her MS in check.

An estimated 400,000 Americans have MS, according to the National Multiple Sclerosis Society (NMSS).

Every week, about 200 people in the United States are diagnosed with the disease. And, like Ferko, many are managing their symptoms and staving off debilitation with medications.

Today, there are six FDA-approved treatments to lessen the likelihood of attacks. Three of them also slow the progression of disability in this often-incapacitating disease.

A Prime-of-Life Disease

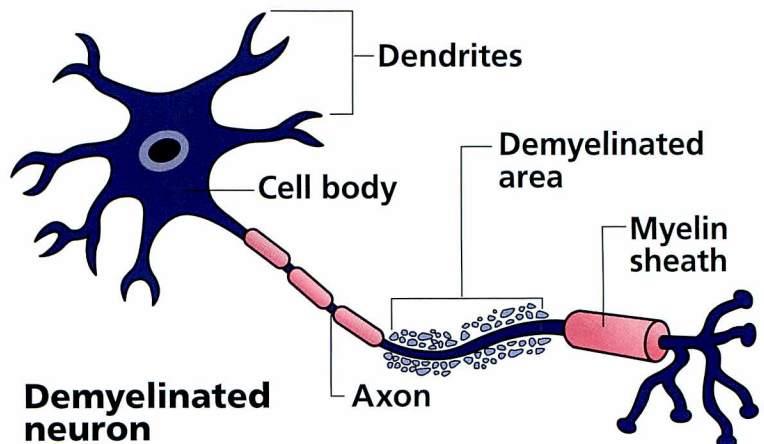
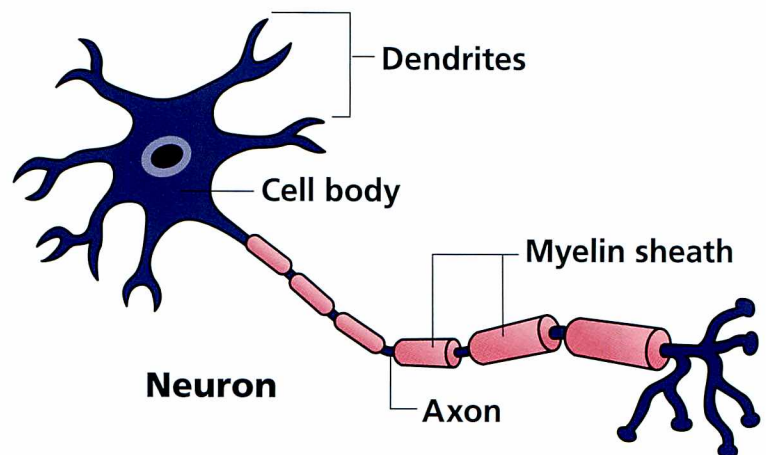
MS is a non-contagious, lifelong chronic disease that causes symptoms

such as weakness, muscle stiffness, poor coordination and balance, tingling, numbness, tremors, blurred vision, and slurred speech. According to the National Institute of Neurological Disorders and Stroke (NINDS), about half of all people with MS also experience memory and concentration problems.

"It's a disease that strikes people typically in the prime of their life," says Susan McDermott, M.D., an FDA neurologist. In rare instances, it can develop in children or older adults,

Healthy vs. Damaged Myelin Sheath

Each nerve cell (neuron) has branchlike extensions (dendrites) that receive messages in the form of electrical impulses from other neurons and a long, slender projection (axon) that transmits messages away from the neuron's cell body. The axon is covered by an insulating fatty layer (myelin sheath). In a healthy person, the protective myelin helps speed message transmissions between the brain, the spinal cord, and the rest of the body. In a person with MS, the myelin is damaged and replaced with scar tissue. These demyelinated areas slow or block communication between neurons.



but MS is diagnosed most frequently in people between the ages of 20 and 50, according to the NMSS.

Ferko's first symptom—loss of vision in one eye—appeared when she was 23. She was diagnosed with inflammation of the optic nerve (optic neuritis), and treatment with steroids restored her sight, she says. It wasn't until five years later that her second symptom appeared—numbness and tingling in one leg. More bouts with optic neuritis and bowel and bladder problems followed, along with mobility problems. "I had a slow, progressive decline in my ability to walk long distances, decreased sensation in my hands, and I would tire easily," says Ferko.

Experts recognize three main forms of MS. In its most common form—relapsing-remitting—an attack, or relapse, is followed by a period of decreased or no symptoms (remission) until the next flare-up. "A relapse can leave some residual disability, or it can

Research indicates that despite disability, most people with MS have a life expectancy only a few years shorter than normal.

Communication Breakdown

The exact cause of MS is unknown. "So many things have been implicated," says McDermott. "The general consensus is that most people who have MS have a genetic predisposition to it, but something in the environment triggers it," such as a virus, bacteria, a toxic chemical, or some other agent. "Gender also seems to play a role," says McDermott, "as women are more commonly affected than men."

Although the disease trigger still eludes researchers, they do know that MS interrupts the body's intricate communication network of nerves. In a healthy individual, nerve fibers act like electrical cables, transmitting electrical impulses, or messages, at high speeds between the brain, the spinal cord, and

Diagnosing MS

MS is "notoriously difficult to diagnose," says Reingold. There is no single test to detect it.

Until recently, to meet the diagnostic criteria for MS, a person must have had two separate attacks at least a month apart and in different parts of the body. But early on in the disease process, some people have infrequent relapses or symptoms so mild that they might not recognize a second attack, says Walton.

In Ferko's case, her eye doctor told her "not to worry about it" after her first symptom, optic neuritis, cleared up. Five years later, another doctor diagnosed her second symptom, leg numbness, as a pinched nerve.

Recent advances in technology, particularly magnetic resonance imaging (MRI), a non-invasive form of taking pictures of the brain to detect MS lesions, have aided physicians in diagnosing people with MS. "Now

The exact cause of MS is unknown.

resolve completely over the course of weeks or months," says Marc Walton, M.D., Ph.D., a neurologist and director of the FDA's Division of Therapeutic Biological Internal Medicine Products.

A second form of MS—primary-progressive—brings on a gradual decline and disability without specific attacks. In the third form—secondary-progressive—MS starts out as relapsing-remitting but eventually takes on a course of gradual progressive disability with few or no relapses.

MS ranges from a very mild, hardly noticeable disease in some people to a very severe, paralyzing disease in others. About 20 percent of people with MS have a benign form of the disease, according to the NINDS. After the first attack, they show minimal, if any, progression and remain fully functional for long periods of time. "However, a majority of people with MS will go on to eventually have significant disability," says Walton.

the rest of the body. The fibers are insulated by a fatty coating called myelin.

In a person with MS, experts say the immune system appears to attack the brain and spinal cord. This attack inflames random patches of plaques, causing lesions that destroy the nerve-protecting myelin. Scar tissue replaces the myelin, a process known as demyelination. When electrical impulses zip through the nerve fibers and reach the scarred areas, they "short circuit," slowing or preventing communication.

The loss of myelin "disrupts the way we receive signals, the way we give commands to our muscles to allow us to move, and the integrating activity that the brain and spinal cord needs to process sensory and motor movement information to allow us to function normally," says Stephen Reingold, Ph.D., research counselor and former vice president for research programs at the NMSS. Continued scarring combined with damage to the nerve fibers may result in permanent disability.

patients can come in with a single clinical episode and a neurologist can use an assortment of lab tools, including MRI, to determine more rapidly than waiting for a second clinical attack if there is a second lesion in the brain or spinal cord," says Reingold.

"This has led to people being given the diagnosis sooner than otherwise," says Walton. "We may now be making diagnoses of MS in more people with the least severe forms. In addition, it is possible that by treating patients earlier, the course of their disease may be less severe."

Highly Variable

One of the frustrations for newly diagnosed patients is the uncertainty of living with a potentially debilitating disease. Dennis Bourdette, M.D., chairman of the neurology department at Oregon Health & Science University in Portland, Ore., describes MS as "highly variable." "In the first few years of the condition, we don't have any way of

confidently identifying individuals who may have a benign course and who will have a more active course."

"There is a series of clues that can help guide us in understanding more about what might happen," says Reingold, "but the variability of the disease from person to person makes giving an individual prognosis for multiple sclerosis very, very uncertain. Most physicians still are uncomfortable with sitting down with a newly diagnosed individual and saying we believe that this may be what is going to be the course of your disease over the next 20 to 30 years."

Relapses also are variable. When they strike, how long they last, and what organs or functions they affect differ from person to person.

"Nobody really knows why relapses occur," says McDermott. In some people, they seem to be triggered by certain events that cause trauma to the

body, she says, such as an accident, surgery, viral infection, or other illness.

Temperature changes may trigger a worsening of symptoms in some individuals. This effect is usually reversible when the temperature returns to normal, but it can sometimes be confused for a clinical relapse. Some people are sensitive to heat, says Reingold, but others are more sensitive to cold. "You need to learn what your disease is like for you, and then you'll learn to cope with it."

Treatment

The FDA has approved six drugs to treat MS, all injections. They cannot reverse the damage already caused by the disease, but they can help prevent relapses and further damage. In addition, a number of oral drugs can help alleviate some of the symptoms, such as fatigue, bladder infections, constipation, pain, depression, and involuntary

jerking movements (spasticity).

The most recent MS drug to hit the market is Tysabri (natalizumab). Licensed by the FDA in November 2004 for people with relapsing forms of MS, Tysabri is the first monoclonal antibody approved for the disease. Monoclonal antibodies are laboratory-produced antibodies similar to those made naturally by a person's immune system to fight infections and other foreign agents in the body.

Tysabri appears to work by adhering to a protein on potentially damaging white blood cells, preventing these cells from traveling from the bloodstream into the brain and spinal cord. "It's a completely different class of molecule and acts in a completely different way from other MS drugs," says Walton.

The FDA approved Tysabri under an accelerated program based on one year of study results instead of the nor-

FDA-Approved Drugs for the Treatment of Multiple Sclerosis

Brand Name	Generic Name	Manufacturer/ Distributor and Year of FDA Approval	Indication (From FDA-Approved Labeling)	Frequency/ Route of Delivery/ Usual Dose
Betaseron	interferon beta-1b	Berlex Laboratories Inc., 1993	Relapsing forms of MS	Every other day; subcutaneous (under the skin) injection; 250 mcg
Avonex	interferon beta-1a	Biogen Idec, 1996	Relapsing forms of MS	Once a week; intramuscular (into the muscle) injection; 30 mcg
Copaxone	glatiramer acetate	TEVA Neuroscience Inc., 1996	Relapsing-remitting MS	Every day; subcutaneous (under the skin) injection; 20 mg (20,000 mcg)
Novantrone	mitoxantrone	Serono Inc., 2000	Worsening relapsing- remitting MS and progressive-relapsing or secondary-progressive MS	Four times a year by IV infusion in a medical facility; lifetime limit of 8-12 doses (12 mg/m ² every 3 months)
Rebif	interferon beta-1a	Serono Inc., 2002	Relapsing forms of MS	Three times a week; subcutaneous (under the skin) injection; 44 mcg
Tysabri	natalizumab	Biogen Idec and Elan, 2004	Relapsing forms of MS	Every four weeks by IV infusion in a medical facility; 300 mg

National Multiple Sclerosis Society

mally required two-year results. A drug is considered for accelerated approval only if it appears to provide a substantial benefit over existing treatments for people with a serious disease. "We granted accelerated approval because the results were so striking they convinced us that it was worthwhile to make the drug available for patients sooner than waiting for the definitive evidence in 2005," says Walton.

In one of two yearlong clinical trials with more than 900 people who have relapsing MS, Tysabri reduced the frequency of relapses by two-thirds compared with an inactive substance (placebo). This means that, on average, among four people receiving the placebo, there were three relapses during the year, while among four people receiving Tysabri, there was only one

breaking free from treatments at times. And one year is a relatively short time compared to the decades that a patient will be taking this drug." As part of the approval, the manufacturers of Tysabri, Biogen Idec Inc., based in Cambridge, Mass., and Elan Pharmaceuticals Inc., of San Diego, have committed to continuing the trials for a second year.

Side effects most frequently observed in the studies of Tysabri included headache, depression, fatigue, joint pains, menstrual disorders, and infections in the urinary tract, lower respiratory tract, gastrointestinal system, and vagina. Serious side effects were uncommon, but those reported most frequently were pneumonia and other infections, gallstones, severe depression, and severe allergic reactions.

Tysabri is injected directly into a vein

iramer acetate), a synthetic drug. All of these drugs reduce the frequency of MS attacks by influencing the activity of the immune system. In addition, Avonex and Rebif may slow down the rate of physical disability.

Each of the four drugs can be injected by the patient at home and each is used at regular intervals, ranging from once a day to once a week. Common side effects of the three interferon drugs are flu-like symptoms and reactions at the area of injection. Copaxone may trigger a short-term reaction that includes flushing, chest pain, heart palpitations, anxiety, and shortness of breath.

Another drug, Novantrone (mitoxantrone), is approved for people with secondary-progressive MS or those with rapidly worsening relapsing-remitting MS. This IV cancer chemotherapy

'The FDA approval of Tysabri creates excitement and caution.'

relapse. Other approved MS drugs have been shown in studies to reduce relapses by about one-third.

A second yearlong clinical trial of nearly 1,200 people involved Tysabri in combination with Avonex (interferon beta-1a), another FDA-approved injectable drug for relapsing MS. The study included people who had been taking Avonex but still had relapses. In this study, relapses were reduced by about one-half in those taking both Tysabri and Avonex. On average, among eight people receiving a placebo while continuing to take Avonex, there were about six relapses during the year. Among eight people receiving Tysabri while on Avonex, there were three relapses.

"We don't know if there is any real benefit to using both Tysabri and Avonex," says Walton. The labeling neither recommends nor discourages the use of Tysabri in combination with another approved drug.

"We are encouraged by the results we have seen," says Walton, but he adds a caution. "In theory, some drugs have the potential to lose their effect over time—the immune system has a way of

(intravenously, or IV) once a month over a period of one hour in a physician's office. "The infusion process is very easy," says Ferko, adding that after the one hour for infusion there is another hour for observation in case of side effects. Ferko says her only side effect was "having a headache within a week of being due to have an infusion," and Tylenol (acetaminophen) helped alleviate her pain.

"The FDA approval of Tysabri creates excitement and caution," says Jack Burks, M.D., a clinical professor at the University of Nevada School of Medicine in Reno, Nev., and vice president and chief medical officer at the Multiple Sclerosis Association of America (MSAA). Burks notes that the drug is not a cure and that some patients still had attacks and ongoing central nervous system damage as indicated by MRI while being treated with Tysabri.

Other Drug Options

Four other treatments for people with relapsing-remitting MS are approved for lifelong use by the FDA: Avonex, Betaseron, and Rebif (beta interferons), and Copaxone (glat-

drug is given in a medical facility. By suppressing the immune system, the drug may reduce new lesions, decrease relapses, and slow down the rate of disability. Because of the serious side effect of heart damage, Novantrone is restricted to use in an individual no more than four times a year for up to three years.

When it comes to choosing a treatment, Reingold says that's a decision for the patient to make with a physician, taking into account the patient's goal, quality of life, lifestyle, and insurance coverage, combined with the physician's perspective on what the best options might be.

"Each of these drugs is different," says Reingold. "They may be different biological molecules. They are given in different doses, they are given at different frequencies, they have different side effect profiles, and they cost different amounts.

"You may or may not be responsive to one drug," he adds, "and you may have allergic reactions or side effects to one drug or not to another drug. There's a certain amount of trial and error. We cannot currently tell at the

onset of treatment which drug is going to be best for which people."

And as far as switching from an older drug to the new Tysabri, Reingold suspects that most physicians won't recommend it if a person is doing well on the older drug until further studies occur that directly compare the effectiveness and safety of the available medications. "There's no reason

sion. Most people learn to recognize that quality of life is more related to having good relationships and feeling productive than running a 100-yard dash."

Doctors advise people with all forms of MS to get enough rest, eat healthily, not smoke, and exercise regularly. "Every person with MS should be on a regular exercise program custom-

functioning of the patients treated with immune therapies from the beginning," says Burks. "What is lost is gone forever."

Harriet Fridkin, 62, knows this all too well. Fridkin knew that something was wrong in 1971, at age 29, when she couldn't hold a drinking glass and her knees buckled under her. She was diagnosed with an orthopedic problem

'We cannot currently tell at the onset of treatment which drug is going to be best for which people.'

to change medications unless there is clear-cut evidence of superior effectiveness or safety in direct comparative studies of Tysabri and other treatments for MS."

As yet, there are no approved treatments for primary-progressive MS. "The currently available drugs focus their actions on inflammation while the damage at this stage is caused from degeneration and not inflammation," says Burks. "Patients with progressive MS can often benefit from rehabilitation therapies such as exercise, nutritional guidance, and psychological support to increase coping and adapting skills plus deal better with depres-

sion. Most people learn to recognize that quality of life is more related to having good relationships and feeling productive than running a 100-yard dash."

Importance of Early Treatment

People who have frequent relapses or whose functioning is severely affected may willingly take one of the injectable drugs approved to treat MS. When symptoms are mild, however, some people are reluctant to go on medication, says Bourdette. But even if a person has just one attack and an abnormal MRI brain scan, "they are at high risk for developing MS," he says, adding that 80 percent to 90 percent of such people will develop MS within five years. "The goal is to make a definite diagnosis as early as possible and go on therapy."

Even without symptoms, "the disease marches on," adds McDermott, noting that studies involving MRIs of the brain of MS patients have shown new lesions forming even when relapses are not occurring. "I've seen patients who say, 'I had a mild attack five years ago and I don't need to be on medication—I'm feeling great.' But the MRI shows a couple new spots, indicating areas of demyelination." It's like hypertension, says McDermott. "You can't feel high blood pressure, but the damage goes on every day."

The patients taking a placebo in clinical trials in MS "never caught up to the

and the symptoms went away after her doctor prescribed several anti-inflammatory drugs. Six years later, Fridkin developed optic neuritis, which cleared up with steroid treatment. It wasn't until 1980, when she was taken by ambulance to a hospital with vomiting, vision problems, and loss of balance, that Fridkin was diagnosed with MS. Treatments at that time were limited and Fridkin was told to "forget about it—you might never get another attack."

When the first interferon drug for MS was approved in 1993, Fridkin's doctor didn't recommend it for her. Looking back, Fridkin believes that earlier treatment may have changed the course of her disease, now in a progressive state. "On a good day, I can move my left arm," says Fridkin, who is confined to a wheelchair.

"Make sure you get help early and are proactive," Fridkin advises people with symptoms, even mild ones. "If a doctor tells you there's nothing you can do, don't be afraid to get a second opinion. Read about the disease, educate yourself, and ask questions."

Fridkin also stresses the importance of exercise but cautions not to overexert. "Don't exercise until you overheat and are tired," she says, "because with MS, you don't recover as fast." Exercising for short periods, more frequently, is less fatiguing, she says.

Drawing on the experiences of people who have had the disease for a long time can also be helpful, says Fridkin.



Biogen Idec Inc.

The first monoclonal antibody approved by the FDA to treat multiple sclerosis is Tysabri (natalizumab). Produced in a lab, monoclonal antibodies are similar to antibodies made naturally by a person's immune system to fight infections.



Photo Researchers Inc.

A woman with multiple sclerosis prepares a syringe to inject herself with Betaseron, one FDA-approved treatment for this disease that attacks the central nervous system.

"Join a support group and listen to what others say." Local support groups and other assistance are available through the NMSS and the MSAA.

Ferko says she is pleased with her quality of life right now. "I haven't been that significantly affected in comparison to many other patients," she says, adding that planning is important. Knowing that early in the day is better for her than afternoons and evenings, Ferko does her physical activities, like grocery shopping, in the mornings and does activities that she can sit down for in the afternoon. "Once you understand your symptoms and how it works in you, you have to modify things a little.

"And one of the most important things you can do is to find a doctor who specializes in MS," Ferko advises. "It made the difference for me."

Future of MS Treatment

Researchers continue to work toward a better understanding of MS and to find safe and effective treatments for all forms of the disease. Current drugs can curtail relapses, but they don't stop the body's attack on its immune system or the degenerative aspect of MS in the more advanced stages. "A major research focus on neuroprotection to stop the degeneration is underway," says Burks.

Another area of research centers on

finding agents that not only stop the damage but also repair it, says Reingold. "We need to learn how to reverse the damage that has been done, and hopefully, to improve functioning on a day-to-day basis for people with MS." Researchers are studying the repair and regeneration of the myelin coating on nerve fibers that is destroyed by MS. "Myelin does repair itself," says Reingold, but myelin repair is then subject to myelin damage in a person with MS whose immune system is launching an attack.

Repairing damage from MS remains a hope for the future, but in the short term, Reingold says, "The general consensus is that no single therapy is going to prove completely efficacious for MS. We need to focus on safety and efficacy of combination therapies and try to capitalize on multiple modes of action." Reingold expects to see more studies that combine drugs with different modes of action, and is encouraged by the explosion of clinical trials. "There are more clinical trials for more new drugs to be used on MS going on right now than ever before in history." ■

For More Information

FDA information on Tysabri
www.fda.gov/cder/drug/infopage/natalizumab/

National Institute of Neurological Disorders and Stroke
 (800) 352-9424
 TTY: (301) 468-5981
www.ninds.nih.gov/disorders/multiple_sclerosis/

National Multiple Sclerosis Society
 (800) FIGHT-MS (344-4867)
www.nmss.org

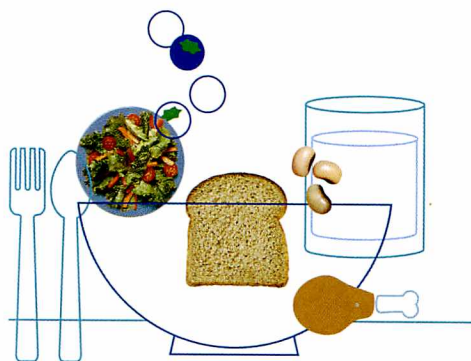
Multiple Sclerosis Association of America
 (800) 532-7667
www.msaa.com

Revised Dietary Guidelines To Help Americans Live Healthier Lives

What should Americans eat?

How should we prepare our food to keep it safe and wholesome?

How should we be active to be healthy?



These questions and others are answered in the latest version of the "Dietary Guidelines for Americans," released in January 2005 by the Department of Health and Human Services (HHS) and the U.S. Department of Agriculture (USDA). The dietary guidelines are the federal government's science-based advice designed to help Americans choose diets that will meet nutrient requirements, promote health, support active lives, and reduce risks of chronic disease.

The guidelines provide the foundation for federal food and nutrition policy and influence the direction of government nutrition programs, including research, labeling, and nutrition promotion.

This newest version of the "Dietary Guidelines for Americans," the 6th edition, is the latest revision of the guidelines, which by federal law must be reviewed every five years.

"These new dietary guidelines represent our best science-based advice to help Americans live healthier and lon-

ger lives," said former HHS Secretary Tommy G. Thompson in announcing the release of the guidelines. "Promoting good dietary habits is key to reducing the growing problems of obesity and physical inactivity, and to gaining the health benefits that come from a nutritionally balanced diet."

Former Agriculture Secretary Ann M. Veneman said, "Taken together, the recommendations will help consumers make smart choices from every food

group, get the most nutrition out of the calories consumed, and find a balance between eating and physical activity."

Eating a healthy balance of nutritious foods continues as a central point in the dietary guidelines, but balancing nutrients is not enough for health. Total calories also count, especially as more Americans are gaining weight. Because almost two-thirds of Americans are overweight or obese, and more than half get too little physical activity, the 2005 guidelines place a stronger emphasis on calorie control and physical activity.

The dietary guidelines are based on what experts have determined to be the best scientific knowledge about diet, physical activity, and other issues related to what people age 2 and older should eat and how much physical activity they need.

"The process we used to develop these recommendations was more rigorous and more transparent than ever before," said Veneman. In the first of a three-stage approach to preparation of the guidelines, a 13-member advisory committee prepared a report based on the best available science. In the second stage, government scientists and officials developed the guidelines after reviewing the advisory committee's report and agency and public comments. Members of the public, including lay people, academic researchers, consumer and trade groups, and businesses, submitted

Don't Give In When You Eat Out

It's important to make smart food choices and watch portion sizes wherever you are—at the grocery store, at work, in your favorite restaurant, or running errands.

Try these tips:

- At the store, plan ahead by buying a variety of nutrient-rich foods for meals and snacks throughout the week.
- When grabbing lunch, have a sandwich on whole-grain bread and choose low-fat or fat-free milk, water, or other drinks without added sugars.
- In a restaurant, opt for steamed, grilled, or broiled dishes instead of those that are fried or sautéed.
- On a long commute or shopping trip, pack some fresh fruit, cut-up vegetables, string cheese sticks, or a handful of unsalted nuts to help you avoid impulsive, less healthful snack choices.

Consider This:

If you eat 100 more food calories a day than you burn, you'll gain about 1 pound in a month. That's about 10 pounds in a year. The bottom line is that to lose weight, it's important to reduce calories and increase physical activity.

comments for the committee and the agencies to consider. In the third stage, experts worked to translate the guidelines into meaningful messages for the public and educators.

The advisory committee's report identifies 41 key recommendations, of which 23 are for the general public and 18 are for special populations. They are grouped into nine general topics:

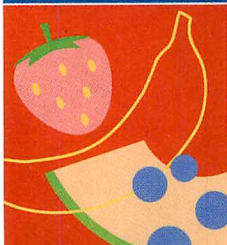
- Adequate Nutrients Within Calorie Needs
- Weight Management
- Physical Activity
- Food Groups to Encourage
- Fats
- Carbohydrates
- Sodium and Potassium
- Alcoholic Beverages
- Food Safety

The dietary guidelines provide health education experts, such as doctors and nutritionists, with a compilation of the latest recommendations. To highlight key points that consumers can apply in their lives, a consumer-oriented brochure accompanies the 2005 guidelines.

The USDA's Food Guidance System also will serve as a tool to educate consumers on the dietary guidelines. The Food Guidance System, which replaces the USDA's 12-year-old Food Guide Pyramid, is being revised and will be released in spring 2005. HHS and the USDA will develop additional materials to help consumers learn about the dietary guidelines and make the recommended healthier choices.

The 2005 guidelines and consumer brochure are available at www.healthierus.gov/dietaryguidelines. ■

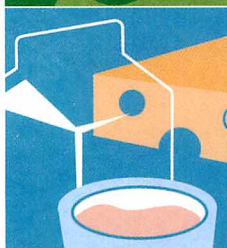
Mix Up Your Choices Within Each Food Group



Focus on fruits. Eat a variety of fruits—whether fresh, frozen, canned, or dried—rather than fruit juice for most of your fruit choices. For a 2,000-calorie diet, you will need 2 cups of fruit each day (for example, 1 small banana, 1 large orange, and 1/4 cup of dried apricots or peaches).



Vary your veggies. Eat more dark green veggies, such as broccoli, kale, or other dark leafy greens; orange veggies, such as carrots, sweet potatoes, pumpkin, and winter squash; and beans and peas, such as pinto beans, kidney beans, black beans, garbanzo beans, split peas, and lentils.



Get your calcium-rich foods. Get 3 cups of low-fat or fat-free milk—or an equivalent amount of low-fat yogurt and/or low-fat cheese (1 1/2 ounces of cheese equals 1 cup of milk)—every day. For kids ages 2 to 8, it's 2 cups of milk. If you don't or can't consume milk, choose lactose-free milk products and/or calcium-fortified foods and beverages.



Make half your grains whole. Eat at least 3 ounces of whole-grain cereals, breads, crackers, rice, or pasta every day. One ounce is about 1 slice of bread, 1 cup of breakfast cereal, or 1/2 cup of cooked rice or pasta. Look to see that grains such as wheat, rice, oats, or corn are referred to as "whole" in the list of ingredients.



Go lean with protein. Choose lean meats and poultry. Bake it, broil it, or grill it. And vary your protein choices—with more fish, beans, peas, nuts, and seeds.

Know the limits on fats, salt, and sugars. Read the Nutrition Facts label on foods. Look for foods low in saturated fats and *trans* fats. Choose and prepare foods and beverages with little salt (sodium) and/or added sugars (caloric sweeteners).



Brain Attack

A Look at Stroke Prevention and Treatment

By Michelle Meadows

As a physical therapist, Dina Pagnotta, 33, has helped more than 100 people recovering from stroke. So when she had a stroke on a May morning in 2002, she had an idea of what was happening.

First, she felt dizzy during a Pilates class in New York City. One moment, she had been laughing with a friend. Then she took a sip of water but couldn't swallow. She choked and the water came right back out of her mouth. Seconds later, she couldn't move her left leg or arm, the left side of her face went limp, and her speech was slurred. "It felt like I got a shot of Novocain in the whole left side of my body," Pagnotta says.

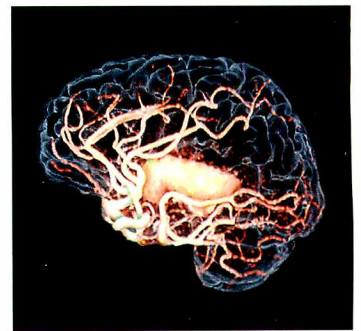


Photo Researchers Inc.

Colored three-dimensional magnetic resonance angiogram (MRA) scan showing a human brain after a stroke, or cerebrovascular accident (CVA). Major arteries are white. The central region (yellow) is an area of bleeding, or hemorrhage.

Dina Pagnotta, a stroke survivor, ran the New York City Marathon in November 2004.

Black Star/Lisa Quiñones

Her friends lowered her to the ground, and someone called 911. "The next thing I knew, I was in an ambulance with the sirens screaming and a paramedic calling it in: '30-year-old female, CVA,'" which stands for cerebrovascular accident, also known as stroke.

A stroke occurs when blood flow to part of the brain is interrupted, which is why it's sometimes called a "brain attack." Pagnotta had an ischemic stroke, the most common kind. It occurs when a blood clot blocks a

recovery and decreasing disability. But the drug must be given within three hours after stroke symptoms begin. It has not been shown to be effective beyond three hours.

"The longer blood flow is cut off and the longer treatment is delayed," Marler says, "the more likely it is that the patient will suffer permanent damage." Stroke experts commonly refer to the sense of urgency in stroke treatment with this expression: "Time is brain."

Marler says, "This is why it's so important to recognize the symptoms

director of the stroke division at New York Presbyterian Hospital at Columbia University. "Stroke may have been prevented if the TIA had been detected and appropriately treated," he says. Doctors may recommend drugs or surgery to reduce the risk of stroke in people who have had a TIA. "For us, TIA is to stroke what chest pain is to heart disease. It's a warning sign that shouldn't be ignored," Sacco says.

The effects of a stroke depend on which area of the brain is affected and how extensive the damage is. One side

When blood flow to the brain stops, brain cells are deprived of oxygen and nutrients.

blood vessel or artery in the brain. Ischemic strokes account for 80 percent of all strokes. Hemorrhagic strokes, which account for the other 20 percent, occur when a blood vessel in the brain ruptures and causes bleeding.

According to the National Institute of Neurological Disorders and Stroke (NINDS), about 700,000 people have a stroke each year—500,000 first strokes and 200,000 recurrent strokes. Stroke is the leading cause of long-term disability and the third-leading cause of death for Americans after heart disease and cancer.

Time is Brain

When blood flow to the brain stops, brain cells are deprived of oxygen and nutrients. "A stroke is a medical emergency because brain cells start dying quickly," says John R. Marler, M.D., a neurologist and associate director for clinical trials at the NINDS. And treatment is most effective when given promptly.

Activase (alteplase), a genetically engineered version of tissue plasminogen activator (t-PA), is the only drug approved by the Food and Drug Administration for treating the sudden onset of ischemic stroke. The drug dissolves blood clots that block blood flow to the brain, improving the chance for

of stroke and call 911 right away." The most common symptoms of stroke are

- sudden weakness or numbness in the face, arms, or legs, especially on one side of the body
- sudden confusion, or difficulty speaking or understanding speech
- sudden vision problems, such as blurry vision or a partial or complete loss of vision in one or both eyes
- sudden dizziness, trouble walking, or loss of balance and coordination
- sudden severe headache with no known cause.

Other symptoms that are less common, but still important, are sudden nausea, vomiting, brief loss of consciousness, or decreased consciousness, such as fainting and convulsions.

Sometimes, people experience a transient ischemic attack (TIA), also called "mini-stroke," which also requires prompt medical evaluation. When a TIA occurs, stroke symptoms may last only temporarily and then disappear. Most TIA symptoms disappear within an hour, but they may persist up to 24 hours.

"About 1 in 4 people who have a TIA go on to have a bigger stroke within five years," says Ralph L. Sacco, M.D., associate chairman of neurology and

of the brain controls the opposite side of the body. So a blood clot on the right side of the brain limits function on the left side of the body and vice versa.

At the hospital, Pagnotta recalls that a doctor kept lifting up her left arm. "Each time, it flopped back down," she says. Pagnotta didn't receive treatment with t-PA. Two hours after her symptoms began, she could move her fingers again, then she could move her whole arm, and her speech improved. After conducting tests, her doctors concluded that there had been a blood clot that temporarily blocked an artery on the right side of her brain, but it dissolved on its own.

"I was lucky," says Pagnotta, who ran the New York City Marathon in November 2004. She is among the roughly 10 percent of stroke survivors who recover almost completely. According to the National Stroke Association (NSA), 25 percent recover with minor impairments, 40 percent experience moderate-to-severe impairments that require special care, 10 percent require care in a nursing home or other long-term care facility, and 15 percent die shortly after the stroke.

Risk Factors

As Pagnotta discovered, stroke can strike without warning. After tests

Blocked or Ruptured Arteries

Ischemic strokes occur because a blood clot blocks an artery or vessel in the brain. Hemorrhagic strokes occur because a blood vessel in the brain ruptures and causes bleeding in the surrounding brain tissue. With ischemic stroke, doctors want to open the artery up and dissolve the clot. With hemorrhagic stroke, they want to clot the blood and stop the bleeding.

Hemorrhagic strokes can be caused by an aneurysm, a thin or weak spot in an artery that bulges and can burst. Other causes include a group of abnormal blood vessels called arteriovenous malformation or leakage from a vessel wall that was weakened by high blood pressure.

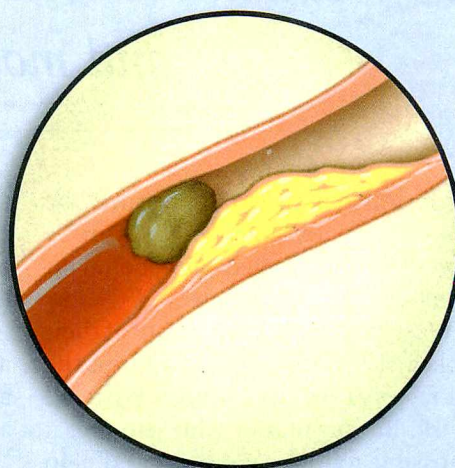
One drug, Nimotop (nimodipine), is approved by the Food and Drug Administration for subarachnoid hemorrhage due to aneurysm. Subarachnoid hemorrhage occurs when a blood vessel ruptures and bleeds into the space between the brain and the skull.

Hemorrhagic stroke is also sometimes treated with surgery that removes abnormal blood vessels or places a clip at the base of an aneurysm. Aneurysms are increasingly being treated by using catheters to place wire coils inside the aneurysm to abolish it.

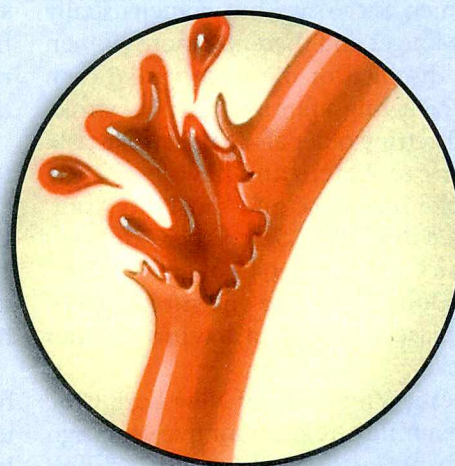
There is no currently FDA-approved treatment for intracerebral hemorrhage, which is when a vessel leaks blood into the brain itself. Joseph Broderick, M.D., chairman of the neurology department at the University of Cincinnati, says this type of stroke kills up to 40 percent of people within about a month after the stroke occurs.

One therapy under investigation is called NovoSeven, which is made by Denmark-based Novo Nordisk. The drug is approved by the FDA for treating bleeding in people with hemophilia, a condition in which a person's blood doesn't clot normally.

In a clinical trial led by Stephan Mayer, M.D., director of the neurological intensive care unit at New York Presbyterian Hospital at Columbia University, NovoSeven has shown promise for stopping early bleeding and improving outcomes in people with intracerebral hemorrhage. ■



Ischemic Stroke



Hemorrhagic Stroke

Phototake

done during a six-day hospital stay, her doctors determined that her stroke likely occurred because of a combination of factors—she had started taking birth control pills for the first time three months earlier and she had a heart problem.

Pagnotta found out that she had a hole in her heart called patent foramen ovale (PFO). She also had an atrial septal aneurysm, a thinning of the wall between the two chambers of her heart. She had an embolic stroke, in which a clot travels to the brain. She says her doctors believe that a blood clot traveled from her heart, through the PFO, to her brain. A blood clot could move to other areas of the body and never pose a problem. But com-

pared with other organs, the brain is much more sensitive to the interruption of blood supply.

A condition called atrial fibrillation also can increase the risk of having an embolic stroke. Normally, the atrium pumps blood into the ventricles, which then sends blood to the rest of the body. In atrial fibrillation, the atrium doesn't pump blood out properly. This increases the likelihood that blood will pool and clot in the atrium. If a piece of that clot breaks off, it can then be pumped to the brain.

Most strokes occur because blood clots develop directly in the brain. These are known as thrombotic strokes. The most common cause is atherosclerosis, a process in which fatty deposits

form in the vessel walls of the brain. The process is similar to what happens in the heart for people with heart disease. This is why stroke and heart disease share some of the same controllable risk factors: high blood pressure, cigarette smoking, high cholesterol, diabetes, physical inactivity, and obesity. These factors raise the risk for plaque build-up in the arteries, which in turn raises the risk of the formation of blockages and blood clots. A stroke sometimes occurs because plaque develops in the carotid artery, the main blood vessel in the neck that leads to the brain.

Sacco says high blood pressure is perhaps the biggest risk factor for stroke. "There are too many people with

'African-Americans have twice the stroke incidence and mortality compared to whites.'

uncontrolled high blood pressure," he says. "Especially given that it can be prevented and treated with behavior changes and medications.

"We want people to be aware of their stroke risk and take steps to address the risk factors they can control. We're all at risk. But no matter who you are, it is possible to lower your risk and help prevent a stroke from happening," Sacco says.

Men have a greater stroke rate than women, Sacco says, but women usually live longer and therefore more women are disabled or die from stroke each year. Having a family history of stroke and getting older also raise stroke risk. "African-Americans have twice the stroke incidence and mortality compared to whites," Sacco says, "and Hispanics also seem to be at greater risk." In addition, having one stroke or TIA increases the risk of having another stroke.

Leslie Virgil, 60, of New York City, had a mild stroke about five years ago with no lasting effects. "So I didn't

think much about it," she says. "But now I see that the first one was like my body telling me: 'Watch out, because the big one is coming.'

"I had high blood pressure, diabetes, and high cholesterol, but I didn't make any changes. My mother had a stroke and so did my mother's brother."

Virgil experienced a second, major stroke in November 2004. Due to a blood clot on the left side of her brain, she lost function in her right leg. Her speech is still slurred. And she has difficulty concentrating and finding the right words to communicate sometimes.

Virgil entered the Rusk Institute of Rehabilitation Medicine, part of New York University Medical Center, in December 2004. She is working with a team of specialists to regain her strength. "My goal is to walk out of here," she says.

Now she takes medication to control blood pressure, cholesterol, and diabetes, and she has switched to a diet that's low in fat, cholesterol, and salt. "This

stroke knocked some sense into me," Virgil says.

Small Window of Opportunity

When the FDA approved Activase (t-PA) in 1996, it was the first drug approved to treat acute ischemic stroke. Made by Genentech of South San Francisco, Calif., the drug is given intravenously to dissolve the clot or clots that are keeping blood from flowing to the brain. It improves the chance of recovery by up to 30 percent when used correctly. But there is a major limitation—the need to begin the treatment within three hours.

"The fraction of people who get treated with t-PA is very, very low, just a few percent of all stroke patients," says Marc Walton, M.D., Ph.D., director of the FDA's Division of Therapeutic Biological Internal Medicine Products. "The three-hour time window is very limiting. There is also a risk of causing intracranial bleeding. Research shows that for safety reasons, doctors are selecting patients carefully."

When someone suffers a stroke, doctors have to run tests to figure out which kind of stroke has occurred and whether the patient is a candidate for t-PA. Meanwhile, time is ticking away. "Hospitals are getting better at evaluating and treating patients with stroke symptoms quickly," Sacco says. "But we also need people to recognize the warning symptoms and get to the hospital sooner."

Most people don't go to the emergency room until more than 24 hours after they experience stroke symptoms, according to the NSA.

James Grotta, M.D., a professor of neurology and stroke program director at the University of Texas Medical School in Houston, says there is a host of reasons for the delay.

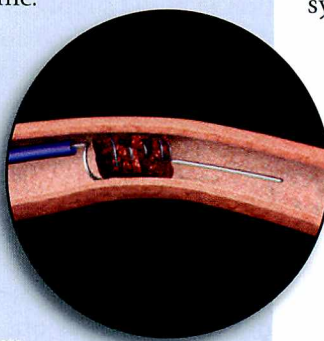
"Some people don't know the signs of stroke," Grotta says. "Other people call their doctor's office or a family mem-

The MERCI Retriever

In August 2004, the Food and Drug Administration cleared the first device to remove blood clots in the brain in people with ischemic stroke. The MERCI Retriever—Mechanical Embolus Removal for Cerebral Ischemia—is made by Concentric Medical Inc. of Mountain View, Calif.

"The device is a catheter with a coiled tip that grasps the clot and allows it to be removed by the physician," says Miriam Provost, deputy director of the FDA's Division of General, Restorative and Neurological Devices. "It may provide an option for some patients who aren't eligible for t-PA."

The risks of the MERCI Retriever include bleeding and vessel punctures. The National Institute of Neurological Disorders and Stroke is funding a clinical trial that continues to study the device. The MERCI Retriever is intended for use by interventional radiologists, doctors who are specially trained to use imaging techniques to view the inside of the body while they guide small instruments through blood vessels to the site of the problem. ■



Concentric Medical Inc.

ber when they should call 911. Some people are embarrassed to call 911 or they go to bed and hope the symptoms will go away. Stroke symptoms also usually don't hurt, which is why some people try to ignore it. And there are geographical challenges when people are far away from a stroke center."

It's a good idea to talk with your doctor about what hospital you should go to if you are at high risk for a stroke, Grotta says. "Consumers should demand good stroke care." The Joint Commission on Accreditation of Healthcare Organizations has recently moved to certify primary stroke centers by requiring them to meet certain criteria. One requirement is that doctors consider administering t-PA.

"It's also important that family members know about stroke symptoms because the stroke victim's thinking may not be clear and the person may not be able to call for help," Grotta says. Les Bissell, 40, who was treated with t-PA after having a stroke in January 2002, credits his girlfriend at the time for getting emergency help so quickly.

Following a vacation, Bissell got up to look at his mail in his Washington, D.C., apartment. Then he walked across the living room and collapsed, breaking a table on the way down. "My legs wouldn't work; they were like jelly," Bissell says.

He tried to get up and came crashing down again, this time taking the TV and stereo with him. His girlfriend had a friend who suffered a stroke a couple of years before and she recognized the signs. After asking him basic questions that he couldn't answer, like his name and where he was, she called 911. "I will always be thankful for her quick action," he says. "If I had been alone, I

probably would have just stayed there on the floor and fallen asleep."

The morning after the stroke, a doctor jingled some keys in front of Bissell and asked him what they were. He had no idea. He was unable to walk or speak. "I could only cry out of fear and frustration," he says. "The alphabet was a complete mystery, although

about prevention and treatment. "Don't let it beat you," Bissell says. "Seek help fast."

Expanding the Options

"The biggest impediment to designing therapy for acute stroke is that the brain is extremely vulnerable," Grotta says. "Brain tissue dies rapidly. The



National Stroke Association

Les Bissell, 40, decided to sail around the world after surviving a stroke in 2002.

it did look vaguely familiar."

Slowly, Bissell recalled letters, words, and names. He got out of the hospital a few days later, and underwent months of speech therapy and physical therapy. He was treated for depression and attended support groups.

He has a slight speech impediment, gets exhausted easily, and has trouble with comprehension. He also has a whole new outlook. Now he lives on a 28-foot boat named HOPE and is sailing around the world to raise awareness about stroke. His voyage began in Annapolis, Md., in April 2004 and he expects to be sailing for three years.

He exchanges e-mails with other stroke survivors and spreads the word

brain is also hard to access. The blood vessels are delicate and tiny, and it's hard to get to the brain with a catheter." One big area of research, he says, involves trying to improve on t-PA.

According to a study published in the Nov. 18, 2004, issue of *The New England Journal of Medicine*, patients who get a combination of t-PA and ultrasound may be able to leave the hospital with a greater chance of recovery. This preliminary study suggests that larger studies to assess the effects on the patient's functional abilities and stroke recovery are worth pursuing.

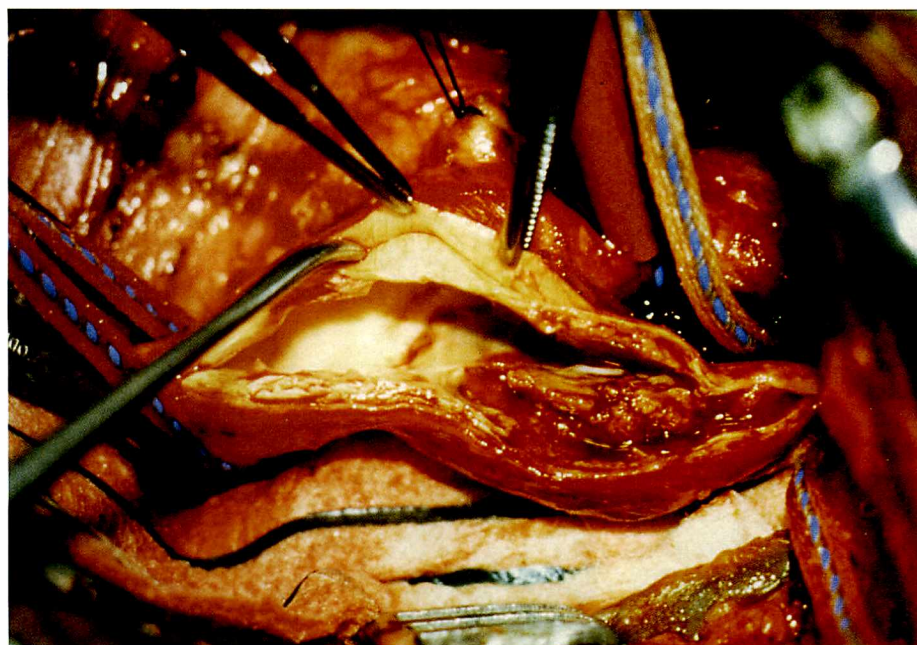
"Ultrasound causes vibrations that work with t-PA to break up clots," says Grotta, who was part of the interna-

tional research team that conducted the study. The team was led by Andrei Alexandrov, M.D., at the University of *Texas-Houston* School of Medicine. Grotta says, "This may help the drug get to the clot and open up blood vessels faster."

Joseph Broderick, M.D., chairman of the neurology department at the University of Cincinnati, says, "We know that t-PA, while a great advance, doesn't really open up the clots fast enough in people with big strokes. We want to find out whether we can do better."

Broderick and his colleagues are studying an approach that combines t-PA with additional treatment through a catheter at the site of the brain clot. Broderick says, "Patients who have already received intravenous t-PA within three hours of onset are taken immediately for intra-arterial angiography, a procedure in which a catheter is inserted into the groin and threaded up to the arteries in the brain." Additional t-PA is put directly into the clot and the catheter is also used to help break up the clot.

"In another NINDS-funded study, we are also comparing t-PA with GP2B3A inhibitors, which are already approved for cardiac use, to see if this combination can open up arteries earlier," Broderick says. GP2B3A inhibi-



National Institute of Neurological Disorders and Stroke

In a procedure called carotid endarterectomy, surgeons remove fatty deposits blocking one of two carotid arteries in the neck. These arteries supply the brain with blood and oxygen.

involves cooling the body to lower body temperature and slow down brain damage due to stroke. Hypothermia can be achieved by inserting cold saline into the body intravenously to cool the body to a certain temperature. The more common method involves external cooling through the skin, such as with "cooling" blankets. "This has been

This experimental treatment is being studied in an NINDS-funded clinical trial.

Preventing Another Stroke

According to the NINDS, about 25 percent of people who recover from a first stroke will have another within five years, and the chance of death and

According to the NINDS, about 25 percent of people who recover from a first stroke will have another within five years ...

tors are agents that prevent platelets in the blood from clumping together.

Researchers are also looking for novel approaches for treating acute ischemic stroke that could be used in addition to t-PA or instead of it. For example, neuroprotective agents protect the ischemic cells from damage or death until blood flow is restored. These agents hold promise, and many have worked in a lab, but none have proven effective in clinical trials.

Hypothermia is another neuroprotective approach under study. This

effective in cardiac arrest patients with brain damage," Grotta says. "It's proof that neuroprotection could work."

Stroke experts say there is also great interest in treatment that could be started much earlier. Jeffrey Saver, M.D., is leading a study at the UCLA School of Medicine that involves treating stroke patients in the ambulance. Paramedics give the potentially neuroprotective agent magnesium sulfate in an attempt to increase blood flow to the brain and prevent buildup of damaging calcium in injured nerve cells.

disability increases with each stroke. The good news is that there is a lot people can do to prevent a recurrence.

Besides lowering stroke risk through lifestyle changes and medication that lowers blood pressure and cholesterol, surgery may be beneficial. In a procedure called carotid endarterectomy, surgeons open up the carotid artery in the neck and scrape out plaque. This is sometimes done for acute stroke, but the procedure has more of a role in preventing recurrent strokes, experts say.

There are two main types of drugs approved by the FDA to prevent a recurrent ischemic stroke.

Surgeons also may open up a clogged carotid artery with a small balloon and insert a small tube called a stent to keep the artery open. In August 2004, the FDA approved the Acculink Carotid Stent System made by Guidant Corp. of Santa Clara, Calif. The stent is intended to prevent stroke by opening a blocked artery. The Acculink is inserted during angioplasty, a procedure in which the

used in those who have had no previous stroke but have a carotid artery that's at least 80 percent blocked and who are not good candidates for the surgical alternative. The FDA is requiring Guidant to conduct post-approval studies to confirm the stent's performance in more patients and to assess its long-term safety and effectiveness.

There are two main types of drugs approved by the FDA to prevent a recurrent ischemic stroke. Antiplatelet drugs, such as aspirin, Plavix (clopidogrel), Ticlid (ticlopidine), and Aggrenox (aspirin and dipyridamole), prevent clotting by decreasing activity of the platelets—the blood cells that make blood clot. These drugs are used to prevent recurrent thrombotic strokes.

Anticoagulants, such as Coumadin (warfarin) and heparin, thin the blood to prevent it from clotting and also prevent existing clots from growing. These drugs are particularly useful in preventing the formation of clots in people with atrial fibrillation.

Pagnotta takes Coumadin every day. She says she bruises easily, which is a side effect of the treat-

Pagnotta says, "The scary part is that I worry every time I have a headache or feel tingling or numbness. I'm wondering is this another stroke?" But this concern has lessened over time.

She is anxiously awaiting the results of a study comparing blood thinners to having her heart condition surgically corrected. "For now," she says, "I'm happy to be alive." ■

For More Information

American Stroke Association
7272 Greenville Ave.
Dallas, TX 75231
(888) 4-STROKE (478-7653)
www.strokeassociation.org

National Stroke Association
9707 E. Easter Lane
Englewood, CO 80112-3747
(800) STROKES (787-6537)
www.stroke.org

National Institute of Neurological Disorders and Stroke
PO Box 5801
Bethesda, MD 20824
(800) 352-9424
www.ninds.nih.gov



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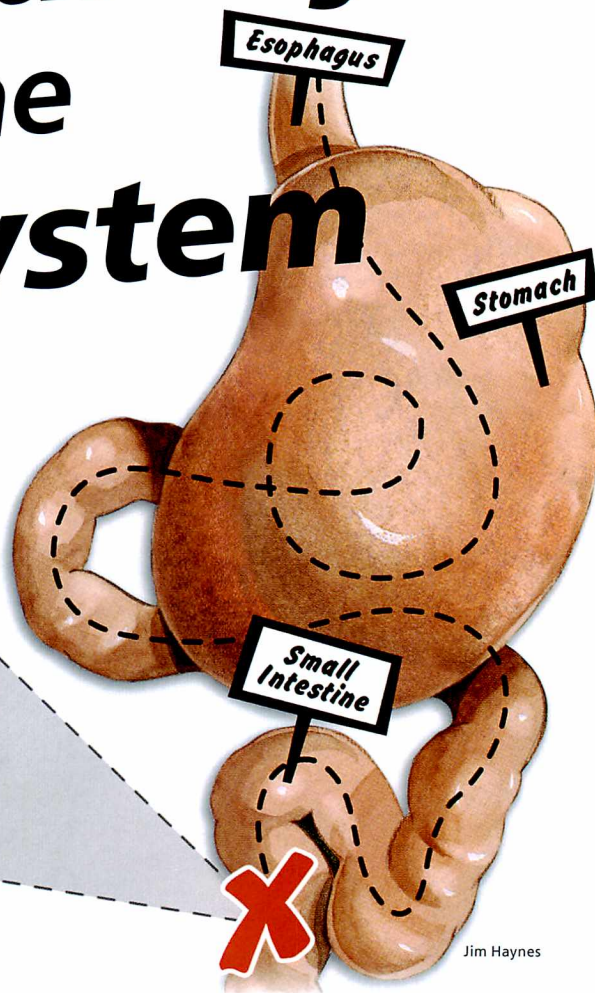
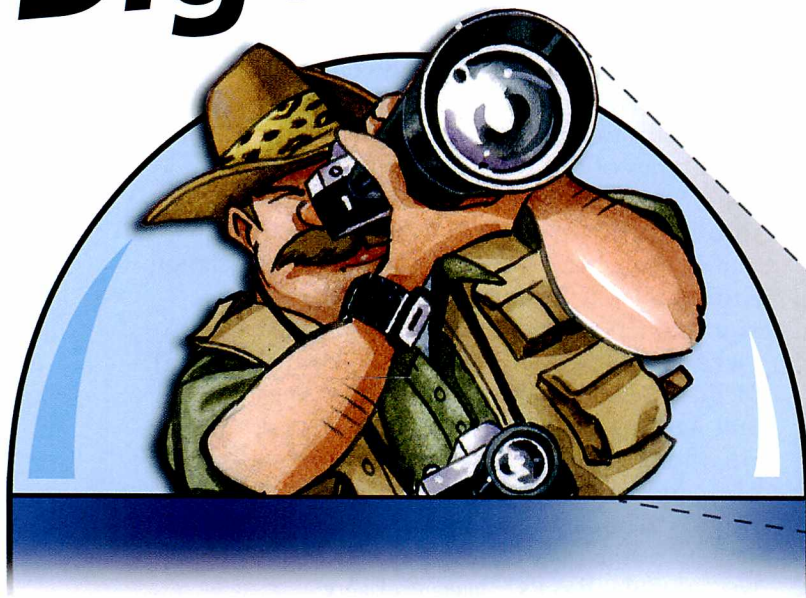
A physical therapist assists a person recovering from stroke.

ment. She also has to be careful to prevent cuts and other accidents because anticoagulants increase the risk of bleeding. She must have her blood levels checked regularly to monitor her risk of clotting and bleeding.

stent is threaded up to the neck artery via a catheter inserted in the groin. The device helps prevent stroke in people who have had a TIA or stroke and who have at least 50 percent blockage of a carotid artery. It also may be

ment. She also has to be careful to prevent cuts and other accidents because anticoagulants increase the risk of bleeding. She must have her blood levels checked regularly to monitor her risk of clotting and bleeding.

Incredible Journey Through the Digestive System



Jim Haynes

By Linda Bren

Lights! Camera! Swallow!

Through the marvels of miniaturization, people with symptoms that indicate a possible problem in the gastrointestinal tract can now swallow a tiny camera that takes snapshots inside the body for a physician to evaluate.

The miniature camera, along with a light, transmitter, and batteries, is housed in a capsule the size of a large vitamin pill. The capsule, called the PillCam, is used in a procedure known as capsule endoscopy, a noninvasive and painless way of looking into the esophagus and small intestine. The procedure requires no sedation and no recovery time, as in a conventional endoscopy where the physician pushes a lighted instrument (endoscope) down the patient's throat to view inte-

rior regions. The disposable PillCam passes naturally and painlessly out of the body in eight to 72 hours.

In November 2004, the Food and Drug Administration cleared the PillCam ESO for use in adults to help detect abnormalities in the esophagus. In 2001, the agency cleared the PillCam SB for detecting problems in the small bowel, or small intestine, in adults and children at least 10 years old. Both types of PillCam are made by Given Imaging Ltd., an Israel-based company with North American headquarters in Norcross, Ga.

Physicians use the PillCam ESO to look for conditions such as gastroesophageal reflux disease (GERD). GERD occurs when a muscle valve in the esophagus malfunctions, allowing stomach acid to flow up into the esophagus and cause heartburn. Left untreated, GERD may lead to a precancerous condition called Barrett's esophagus.

Blair Lewis, M.D., a gastroenterologist at Mount Sinai School of Medicine in New York City, notes that the PillCam ESO views only the esophagus—not the stomach or the beginning of the small intestine where peptic ulcers may form. "It does not replace conventional endoscopy," Lewis says, because endoscopy allows the physician to view these areas and to take a tissue sample (biopsy). If a capsule endoscopy suggests a serious problem, the patient will still need conventional endoscopy to confirm a diagnosis, he says.

Lewis uses the PillCam ESO for patients "who are reticent to have an upper endoscopy but are still concerned that they may develop problems such as Barrett's esophagus." Capsule endoscopy, as with traditional endoscopy, can help guide treatment, he says.

The PillCam SB, which views the small intestine, can help determine the cause of persistent abdominal pain,

unexplained rectal bleeding, or diarrhea. Physicians use it to detect polyps, cancer, and other causes of bleeding and anemia, such as Crohn's disease, a chronic inflammation of the digestive tract that can cause abdominal cramps, diarrhea, and anemia.

"[The PillCam] can see lesions that indicate sources of gastrointestinal bleeding," says Jamie Barkin, M.D., professor of medicine at the University of Miami and chief of gastroenterology at Mount Sinai Medical Center in Miami Beach, Fla. "Crohn's disease is not apparent on X-rays," he says, "so it can find Crohn's at an earlier stage and tell us the extent of Crohn's."

"The advantage of capsule endoscopy is that it sees areas that were never seen before—areas that were overlooked by conventional endoscopy and small bowel X-ray," adds Barkin. Only about 20 percent of the small intestine can be seen with conventional endoscopy, he says.

The PillCam SB allows doctors to see the entire 20-foot-long small intestine; however, it does not photograph the large intestine—the site of colon cancer. "It doesn't replace the colonoscopy," says Jeffrey Cooper, D.V.M., an FDA medical officer who evaluated the PillCam. "The battery has an eight-hour life expectancy, which generally is long enough to photograph the small intestine but not the entire gastrointestinal tract," he says.

The Procedure

A person must fast for 10 hours prior to undergoing capsule endoscopy for the small intestine, but can eat four hours after swallowing the capsule. Lewis says he schedules patients early in the morning, so they can eat lunch and dinner. Wire leads with sensors on the end are affixed to the patient's abdomen and connected to a data-recording device worn on a belt around the waist.

The PillCam SB takes about eight hours to move through the small intestine,

taking two pictures per second with its single camera. During this time, the person can leave the doctor's office and go about a regular routine while wearing the sensors and recorder. Later, the person returns to hand over the sensors and data recorder. The physician downloads about 57,000 color images into a computer, which compresses them to form a video. The physician then views the video on a monitor to determine the next step in treatment.

A two-hour fast is required before taking the PillCam ESO, which views the esophagus. Wire leads with sensors are placed on the patient's chest and connected to a recording device. The person swallows the capsule with water while lying flat on the back. Every two

at either end, to take about 2,600 total color images of the esophagus.

Few Side Effects

The FDA clearance of the PillCam devices was based on their safety, ability to detect abnormalities in the small intestine and esophagus, and lack of side effects.

No cramping or discomfort has been reported with the PillCam, says Lewis, who has conducted clinical studies involving the device. People have "no clue it's there," he says, adding that he's gotten calls from some patients who insisted that it did not pass in their stool and requested an X-ray to confirm it was no longer there.

The size of the capsule—a little more than an inch long and a little less than one-half inch wide—may be daunting for some individuals. "Children and people who have trouble swallowing pills may have a hard time swallowing the capsule," says Cooper.

"Once inside, if a patient has a small blockage, the device could get hung up, sometimes requiring surgery to remove it," he says. The device is not for use in a person with a known intestinal blockage or a significantly narrowed small intestine.

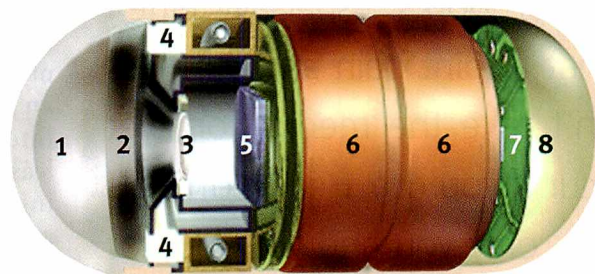
Lewis notes that, in studies worldwide involving a total of 150 patients, the esophageal capsule never became lodged in the body.

In larger studies, the capsule for the small intestine became lodged in the gastrointestinal tract in less than 1 percent of those studied.

Most insurance carriers will reimburse patients for the capsule endoscopy for the small intestine, says Lewis. However, the newer esophageal capsule endoscopy is not yet widely accepted by carriers, who consider it on a case-by-case basis.

To find a physician who uses capsule endoscopy, see the physician locator at www.givenimaging.com. ■

Inside the PillCam



- | | |
|--------------------------|----------------|
| 1. Optical Dome | 5. Imager |
| 2. Lens Holder | 6. Battery |
| 3. Lens | 7. Transmitter |
| 4. Light-Emitting Diodes | 8. Antenna |

Given Imaging

minutes over a six-minute period, the person is raised by 30-degree angles until sitting upright, then remains upright for an additional 15 minutes to make sure the capsule has traveled through the entire esophagus.

The gradual rise to a sitting position slows down the movement of the PillCam ESO, giving it additional time to take pictures. In contrast to the PillCam SB, which moves slowly through the snake-like turns of the small intestine over several hours, the PillCam ESO "moves through the esophagus in minutes," says Cooper. Given Imaging added a second miniature camera to the ESO capsule, putting one camera

Helpful Treatments Keep People With Arthritis Moving

By Carol Rados

Few people with arthritis would be willing to stop taking a medication that works, especially when nothing else has. But what if joint pain and stiffness are inevitable if you don't take the medication, yet heart problems could occur if you do? Health officials say that, as with any drug, only you and your doctor can determine the level of risk that is acceptable with medications currently available to treat arthritis.

The unsettling news in late 2004 that the popular anti-inflammatory arthritis drugs Vioxx (rofecoxib), Celebrex (celecoxib), and Bextra (valdecoxib) could cause a heart attack or stroke or aggravate high blood pressure has left some patients wondering whether they should keep taking them.

Data from clinical trials showed that cyclooxygenase-2 selective agents, better known as COX-2 inhibitors, may be associated with an increased risk of serious cardiovascular problems, especially *when used in high doses or for long periods in patients with existing cardiovascular disease, or in very high-risk situations, such as immediately*

after heart surgery. COX-2 inhibitors are the newest subset of non-steroidal anti-inflammatory drugs (NSAIDs). COX-2 inhibitors were developed specifically to decrease the well-recognized gastric side effects and intolerance associated with the use of some NSAIDs.

Traditional NSAIDs, such as aspi-

rin or ibuprofen, act by blocking the production of a family of chemicals known as prostaglandins, which are not only important in the development of inflammation, but also play an important role in maintaining the integrity of the stomach lining. At least two enzymes are involved in this inflammation, namely cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2). Traditional NSAIDs inhibit both COX-1 and COX-2. Unfortunately, this non-selective inhibition of both COX enzymes also inhibits those prostaglandins involved in some of the important "housekeeping" functions of the body, such as helping blood to clot and protecting the stomach from ulceration.

It is this non-selective inhibition of both enzymes by aspirin and other non-selective NSAIDs that increases the risk of stomach ulcers and consequent bleeding. In theory, the newer COX-2 selective inhibitors only inhibit the enzyme involved in inflammation, leaving the other functions alone.

But Sandra Kweder, M.D., deputy director of the Food and Drug Administration's Office of New Drugs, says that new studies have had a surprising twist. "The downside of the COX-2 selective inhibitors is that they appear to be associated—particularly when used for many consecutive months to years—with an increased risk of



Getty Images

cardiovascular problems," she says. Moreover, COX-2 inhibitors, like other NSAIDs, don't influence the course of the disease—which doctors say is a common misconception among patients—because these drugs only provide for symptom relief.

Coincidentally, preliminary results from a three-year trial on the non-selective NSAID Aleve (naproxen) also suggested that long-term use may be associated with an increased risk for cardiovascular problems.

Since the results of studies on both non-selective and selective NSAIDs

are preliminary and conflict with data from earlier studies of the same drugs, the FDA issued a public health advisory in December 2004 concerning use of all NSAIDs, pending further review of data that continue to be collected. The agency has recommended, among other things, that physicians limit the use of COX-2 inhibitors until further review.

"Monitoring the drug safety of marketed products requires close collaboration between our clinical reviewers and drug safety staff to evaluate and respond to adverse events identified in

ongoing clinical trials or reported to us by physicians and their patients," says Kweder. "The most recent actions concerning [NSAIDs] illustrate the vital importance of the ongoing assessment of the safety of a product once it is in widespread use."

Others Weigh In

The concerns with the safety of so many pain relievers used to treat arthritis underscores the importance of arthritis as a major health care issue in the United States. Arthritis experts, patient advocacy groups, and other health organizations also are weighing in on the uncertainty of NSAIDs, and are recognizing the need for developing new and safer medications.

The American College of Rheumatology is advising physicians to follow current treatment guidelines and manufacturers' dosage recommendations for NSAIDs. Treatment guidelines exist to help doctors choose the best options for their patients, based on current scientific studies.

The Arthritis Foundation said in a statement that the findings about the drugs should not have any immediate impact on the clinical use of them.

"Non-steroidal anti-inflammatory drugs continue to play an important role in the management of arthritis pain," says John H. Klippel, M.D., president and CEO of the Arthritis Foundation. "Patients who derive benefit from these drugs should remain on their treatment regimen, and discuss concerns with their physicians," he says.

But Charles A. Birbara, M.D., a rheumatologist and associate professor of medicine at the University of Massachusetts Medical School in Worcester, Mass., says that he has prescribed COX inhibitors cautiously in older people or those with cardiovascular or renal disease ever since early clinical studies discovered a possible risk in this patient population.

"I'm not always willing to take a risk with my patients, because we clearly don't have a complete understanding of all the potential clinical issues associated with use of these drugs," he says. Even before the controversy, Birbara notes that the long-term effects of COX-2 agents were unknown. Besides,

he says, there are other treatment options available that are equally effective.

"There are so many wonderful things happening with respect to current therapies of arthritis," he says. "Clearly, we are so much better able to control inflammatory arthritis with new biologic agents." Birbara adds that so many people whose lives were diminished by joint disease can now look forward to an unrestricted lifestyle, which was "not even imaginable just a few short years ago."

Richard Shirley, 64, an avid bird-watcher from Wrentham, Mass., battled rheumatoid arthritis in nearly every joint in his body for more than

only in the United States, but for the entire world.

The Burden of Arthritis

Although the clinical term literally means joint inflammation, "arthritis" actually refers to a group of more than 100 rheumatic conditions. According to the Centers for Disease Control and Prevention (CDC), self-reported doctor-diagnosed arthritis collectively affects nearly 43 million Americans—or about 1 in 5 adults. Another 23 million have chronic musculoskeletal symptoms that suggest they, too, may have arthritis. This makes arthritis one of the most common illnesses in the United States and a leading cause of

joint is inflamed, it may be swollen, tender, red, or warm to the touch. In a healthy joint, the ends of the bones are covered by cartilage, a spongy material that allows almost frictionless motion between bones. In fact, Birbara says the amount of heat produced when bones normally meet is less than when two pieces of ice are rubbed together. The joints are enclosed in a capsule and lined with tissue called the synovium. This lining releases a slippery, lubricating fluid that helps the joint move smoothly and easily. Muscles and tendons support the joint and help it move. With arthritis, the cartilage may be damaged or worn away by degenerative processes or by inflammation,

Some rheumatic diseases are systemic, meaning they can affect the whole body.

25 years before he saw Birbara. He couldn't button his shirt cuffs, walk frontward down a flight of stairs, or get in and out of a car without a struggle. At times, his hands were so swollen he couldn't grasp small objects or make a closed fist. Shirley had his wedding ring resized so it would fit.

"Richard had seen a number of physicians and had been on many medications to treat his disease," Birbara says. "However, the aggressive nature of his arthritis was not very responsive to standard medications." According to Birbara, X-rays of Shirley also showed evidence of joint destruction.

"Doctor Birbara has a zero tolerance for hot and inflamed joints," Shirley says, "because that's when the damage is done." Shirley also believes, from his own experience, that each person needs to work with his or her physician to find the appropriate medicine. For him, a new biologic product made the difference.

Finding the right treatments for those at greatest risk for the potential complications of arthritis and other rheumatic conditions, Birbara says, hopefully will lessen the burden of this disease, not

disability. As the population ages, the CDC says that the number of Americans affected will increase dramatically.

"People ignore arthritis both as public and personal health problems because it doesn't kill you," says Capt. Charles G. Helmick, M.D., a medical epidemiologist at the CDC. "But what they don't realize is that, as people work and live longer, arthritis can affect their quality of life and lead to limitations in activities and work and eventually disability."

Arthritis limits everyday activities for 8 million Americans, according to statistics compiled by the CDC. Each year, arthritis results in 750,000 hospitalizations and 36 million outpatient visits. In 1997, medical care for arthritis cost over \$51 billion. The disease affects people of all ages. Nearly two-thirds of those with arthritis are younger than 65. Arthritis may affect people of all racial and ethnic groups. It is more common among women and older Americans.

Arthritis symptoms include joint pain, stiffness, inflammation, and limited movement of joints. When a

making movement painful and difficult. If left undiagnosed and untreated, arthritis may progress to cause irreversible damage to the joints.

Some rheumatic diseases are systemic, meaning they can affect the whole body. Diseases such as systemic lupus erythematosus (SLE) can cause arthritis as well as damage to virtually any bodily organ or system, including the heart, lungs, kidneys, blood vessels, skin, and brain, and may result in debilitating, and often life-threatening, complications.

According to the Arthritis Foundation, the most common form of the disease—osteoarthritis (OA)—affects about 21 million people in the United States. Also called "degenerative joint disease," OA is caused by the breakdown of cartilage and bones from the wear and tear of life, resulting in pain and stiffness. OA usually affects weight-bearing joints such as the knees and hips, but an inherited form commonly affects the hands and spine. Pain and stiffness are the earliest symptoms in OA, which affects both men and women and usually occurs after age 45. Other risk factors include joint



Black Star/Dana Smith

After experiencing many years of pain and inflammation from rheumatoid arthritis, Richard Shirley finally found relief with periodic injections of an FDA-approved biological treatment.

trauma, obesity, and repetitive joint use. In most cases, OA can be detected by X-rays. Treatments include medications, education, physical activity or exercise, heat or cold, joint protection, pacing activities, weight loss if overweight, self-care skills, and sometimes surgery.

Shirley has the second most common type—rheumatoid arthritis (RA)—an autoimmune disease that occurs when the body's immune system mistakenly attacks the synovium and can lead to damage of both cartilage and the adjacent bone. RA may affect any joint but most commonly starts with inflammation in the hands and feet.

While the cause remains elusive, doctors suspect that genetic factors are important in RA. Recent studies

have begun to tease out those specific genetic characteristics that make a person susceptible to developing RA. However, the inherited trait alone does not appear to fully account for the development of the illness. Researchers think this trait, along with some other unknown factor—probably in the environment—triggers the disease.

But RA can be difficult to diagnose early because it may begin gradually with subtle symptoms that usually wax and wane. According to the Arthritis Foundation, this form of arthritis affects more than 2 million people in the United States and is more common in women than men. Ironically, even when the disease appears to be relatively inactive—as measured by the patient's pain, swelling, and stiff-

ness—joint deterioration is likely to be progressing.

In early disease, most of the disability that patients experience is due to inflammation. In later disease, however, it is the loss of joint integrity that creates disability. This often necessitates surgical joint reconstruction or replacement procedures. Treatments for RA also include medications, exercise, rest, joint protection, and self-care skills.

Managing Arthritis and Rheumatic Conditions

For years, the pain and inflammation of arthritis have been treated using medications, local steroid injections, and joint replacement—all with varying success. Seldom did the therapies make the pain go away completely or for very long, nor did they affect the underlying joint damage.

Today's researchers are working to improve diagnostic tools and develop treatments to forestall joint erosion. Even people whose joints are already damaged by arthritis can benefit from the knowledge generated by today's research. Patients should consult with their doctors to determine which treatments are the most appropriate for their conditions.

Most arthritis medications fall into three categories: those that relieve pain; those that reduce inflammation or the body process that causes swelling, warmth, and redness; and those that slow the disease process and limit further damage to the joints—so-called disease-modifying agents.

Pain relievers such as Tylenol (acetaminophen) and NSAIDs such as Motrin (ibuprofen) are used to reduce the pain caused by many rheumatic conditions. NSAIDs have the added benefit of decreasing the inflammation associated with arthritis. But a common side effect of NSAIDs is stomach irritation, which can often be reduced by changing the dosage or medication. Even acetaminophen has risks when taken in large doses, Kweder says.

Before safety concerns about Vioxx, Celebrex, and Bextra emerged in December 2004, these newer COX-2 NSAIDs were used primarily to reduce gastrointestinal side effects and offered

an additional option for treatment.

Depending on the type of arthritis, a person may use a disease-modifying anti-rheumatic drug (DMARD). This category includes several unrelated medications that are intended to slow or stop disease progress and prevent disability and discomfort. DMARDs include Rheumatrex (methotrexate), Azulfidine (sulfasalazine), and Arava (leflunomide).

Someone diagnosed with RA today is likely to be prescribed a DMARD fairly early in the course of the disease, as doctors have found that starting these drugs early can help prevent irreparable joint damage that might otherwise occur.

Corticosteroids, such as prednisone, cortisone, methylprednisolone, and hydrocortisone, are used to treat many rheumatic conditions because they decrease inflammation and sup-

ture systems. Conventional drugs are chemically synthesized. Of the four currently licensed biologics, three help reduce inflammation and structural damage of the joints by blocking a substance called tumor necrosis factor (TNF), a protein involved in immune system responses. Elevated levels of TNF are found in the synovial fluid of rheumatoid and some other arthritis patients.

The first biologic to receive FDA approval for patients with moderate-to-severe RA was Enbrel (etanercept). Initially, it was taken twice weekly by injection, but a once-weekly preparation is now available. Enbrel has been shown to decrease pain and morning stiffness and improve joint swelling and tenderness. In 2000, the drug's approved uses were expanded to include delaying structural damage. Besides RA, Enbrel now has been

able cytokine receptor, which means it is similar in structure to protein molecules found attached to the surface of cells that bind TNF. Enbrel competes with these receptors to inhibit them from binding TNF, thus blocking them from setting off the immune process responsible for RA, psoriatic arthritis, and ankylosing spondylitis.

Siegel warns that caution is important when using these agents as treatments. "All TNF blockers are associated with infection," he says.

Kineret (anakinra), another biologic approved by the FDA for patients with RA, has been shown in clinical trials to improve pain and swelling and slow the progression of structural damage in patients.

Arthritis Treatment Devices

Two medical device products, Hyalgan and Synvisc, are preparations that

Heat and cold can both be used to reduce the pain and inflammation of arthritis.

press the immune system. The dosage of these medications will vary depending on the diagnosis and the patient. Corticosteroids can be given by mouth or by direct injection into a joint or tendon sheath.

For Shirley, any minor relief he experienced over the 25 years was due to injections of corticosteroid preparations into his joints. The injections would relieve his pain, stiffness, and swelling temporarily. Unfortunately, corticosteroids given orally and for prolonged periods and at higher doses may carry side effects such as brittle bones, cataracts, elevated blood sugar, and an increased susceptibility to infections throughout the body.

Biologic Treatments

Biological products are a relatively new class of drugs used for the treatment of RA. Biologics differ from conventional drugs in that they are derived from living sources, such as cell cul-

ture systems. Conventional drugs are chemically synthesized. Of the four currently licensed biologics, three help reduce inflammation and structural damage of the joints by blocking a substance called tumor necrosis factor (TNF), a protein involved in immune system responses. Elevated levels of TNF are found in the synovial fluid of rheumatoid and some other arthritis patients.

The two other TNF-blocking products approved to treat RA are Remicade (infliximab) and Humira (adalimumab), a drug that provided the long-awaited relief for Shirley through a 2002 clinical trial. All three TNF blockers have been demonstrated to improve physical function in studies of at least two years in duration.

"While all three inhibit the action of TNF," says Jeffrey N. Siegel, M.D., team leader for the FDA's Division of Therapeutic Biological Internal Medicine Products, "they do it in somewhat different ways." Remicade and Humira are monoclonal antibodies, laboratory-produced proteins similar to those made by a person's immune system that bind and remove TNF from the body before it can set off the immune reaction responsible for RA.

Enbrel, on the other hand, is a solu-

tion of a naturally occurring body substance that lubricates the knee joint called hyaluronic acid. The products, which were approved by the FDA for the treatment of OA of the knee, are injected directly into the knee joint to help provide temporary relief of pain and flexible joint movement.

Another device used in arthritis treatment is transcutaneous electrical nerve stimulation (TENS), which has been found effective in modifying pain perception. TENS blocks pain messages to the brain by directing mild electric pulses to nerve endings that lie beneath the painful area of the skin.

A blood-filtering device called the Prosorba Column is used in some cases for filtering out harmful antibodies in people with severe rheumatoid arthritis.

Heat and cold can both be used to reduce the pain and inflammation of arthritis. Patients and their doctors can determine which one works best.

Thanks to the right treatment, Shirley says his pain level today is only about 10 percent of what it once was. "Looking back on those days," he says, "it's hard to believe all the things I can do now. I've regained mobility and strength." And once again, Shirley can mow the lawn, cook meals, fix things around his house, and even pursue his favorite hobby of bird watching.

"Rheumatoid arthritis is now an illness for which newer treatments offer the real likelihood of patients being able to pursue a lifestyle without the limitations imposed by joint pain and deformity," adds Birbara.

Importance of Diet and Exercise

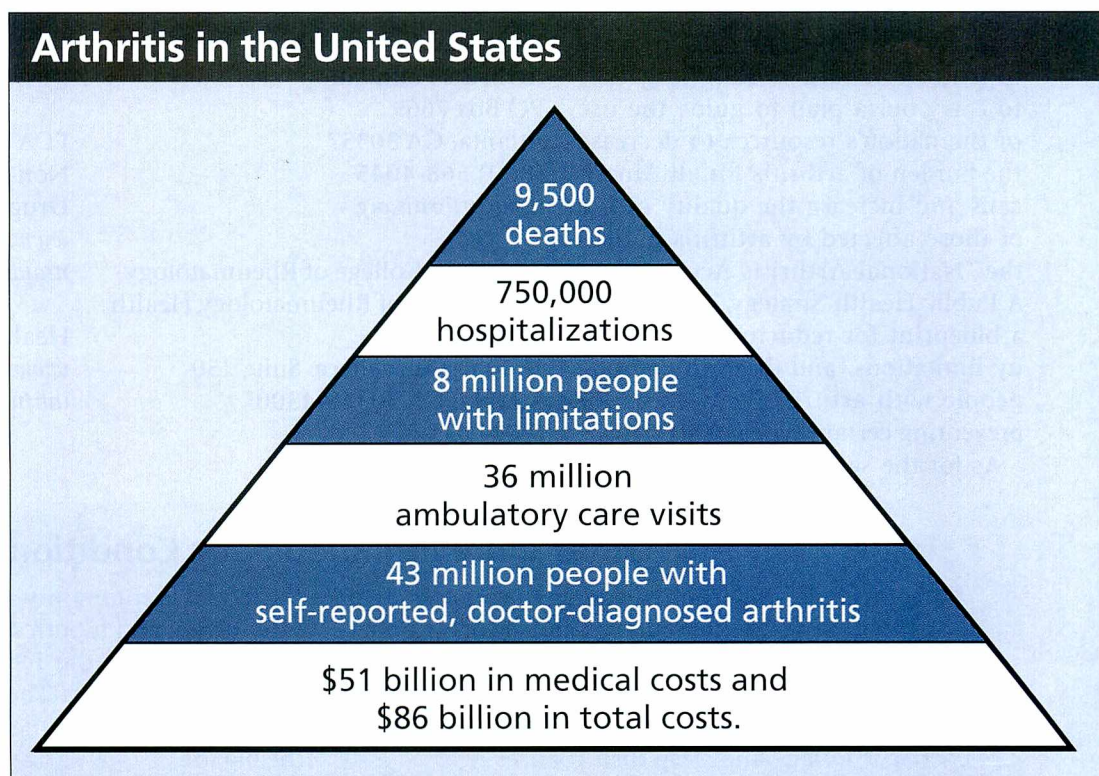
Arthritis experts say there's value in physical activity, the right diet, and other non-medicinal interventions that can help prevent arthritis, reduce pain, and keep people moving, as emphasized in a 10-year initiative called Healthy People 2010. A comprehensive, nationwide health promotion and disease prevention program developed by the Department of Health and Human Services, Healthy People 2010 contains 467 objectives for improving the nation's health in conditions such as cancer, sexually transmitted diseases, and arthritis.

Research in 2004, for example, demonstrated that exercise and diet together significantly improve physical function and reduce knee pain in people older than 60 who are overweight or obese, according to both the Arthritis Foundation and the American College of Rheumatology. The results of the study are published in the May 2002 issue of *Arthritis & Rheumatism*. Similarly, pain and disability accompanying all types of arthritis can be minimized through early diagnosis and appropriate management, including self-management, physical and occupational therapy, joint replacement surgery, weight control, and physical activity.

According to the CDC, research shows that physical activity decreases joint pain, improves function and a person's mood and outlook, and delays disability. Exercise helps reduce the pain and fatigue of many different kinds of arthritis and helps people work and do daily activities and remain independent. Range-of-motion, strengthening, and endurance exercises, such as moving a joint as far as it will go, using muscles without moving joints, and aerobic exercises,

arthritis and decreases disease progression.

Some people claim to have been cured by treatment with herbs, oils, chemicals, special diets, radiation, or other products. According to the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), however, there is no scientific evidence that such treatments cure arthritis. Moreover, some of these unproven treatments may lead to serious side effects. Patients should talk to



Centers for Disease Control and Prevention

respectively, are beneficial in decreasing fatigue, strengthening muscles and bones, increasing flexibility and stamina, and improving the general sense of well-being.

It's important that people stay at their recommended weight, especially as they get older, because being overweight makes them more at risk for OA. Extra weight increases the risk for getting OA in the knees and possibly in the hips. This is especially true for women. In men, extra weight increases the risk for getting another common form of arthritis, gout (excess uric acid in the blood), as well. Maintaining a healthy weight and avoiding joint injuries reduces the risk of developing

their doctors before using any therapy that has not been prescribed or recommended by their health care team.

Juvenile Arthritis

Nearly 300,000 children in the United States have a form of juvenile arthritis or a rheumatic disease that occurs before age 16. The most common form in children is juvenile rheumatoid arthritis. The cause of most forms of juvenile arthritis remains unknown. Juvenile arthritis is not contagious, and there is no evidence that foods, toxins, allergies, or vitamin deficiencies play a role. Current research indicates that there may be a genetic predisposition to juvenile arthritis. In other words, the combina-

tion of genes a child inherits may contribute to the development of arthritis when combined with other undefined factors. Most of the symptoms of juvenile arthritis are due to inflammation as a result of imbalances in the immune system. Despite not knowing the exact cause or causes, there are many effective treatments available to help children and their parents manage juvenile arthritis. Experts say that most children with arthritis can expect to live normal lives.

The Future

Many government and private organizations are working together to carry out a plan to guide the use of the nation's resources to decrease the burden of arthritis for all Americans and increase the quality of life of those affected by arthritis. Called the "National Arthritis Action Plan: A Public Health Strategy," it provides a blueprint for reducing pain, activity limitations, and disability among people with arthritis, as well as for preventing certain types of arthritis.

As for the safety of future arthritis

treatments, experience has shown that the full magnitude of some potential risks of all drugs has not always emerged during the mandatory safety and effectiveness studies conducted before the FDA can approve a drug. As always, the agency advises physicians to consider the evolving information on any medication in evaluating the risks and benefits of these drugs in individual patients.

"The outlook for people with arthritis has never been more hopeful," adds Birbara. ■

For More Information

Arthritis Foundation
PO Box 7669
Atlanta, GA 30357
(800) 568-4045
www.arthritis.org

American College of Rheumatology
Association of Rheumatology Health Professionals
1800 Century Place, Suite 250
Atlanta, GA 30345-4300
(404) 633-3777
www.rheumatology.org

National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)
1 AMS Circle
Bethesda, MD 20892-3675
(877) 226-4267 (toll free)
www.niams.nih.gov

Centers for Disease Control and Prevention
National Center for Chronic Disease Prevention and Health Promotion
Mail Stop K-45
4770 Buford Highway, N.E.
Atlanta, GA 30341-3717
(770) 488-5464
www.cdc.gov/nccdp/hp/

FDA Public Health Advisory
Non-Steroidal Anti-Inflammatory Drug Products
www.fda.gov/cder/drug/advisory/nsaids.htm

Healthy People 2010
www.healthypeople.gov/Document/html/uih/uih_1.htm

Other Common Rheumatic Conditions

Fibromyalgia—a chronic disorder that causes pain throughout the tissues that support and move the bones and joints. Pain, stiffness, and localized tender points occur in the muscles and tendons, particularly those of the neck, spine, shoulders, and hips. Patients also may experience fatigue and sleep disturbances.

Systemic lupus erythematosus (lupus or SLE)—an autoimmune disease in which the immune system harms the body's own healthy cells and tissues. This can result in inflammation of and damage to the joints, skin, kidneys, heart, lungs, blood vessels, and brain.

Scleroderma (systemic sclerosis)—affects the skin, blood vessels, and joints and literally means "hard skin." It may also affect internal organs, such as the lungs and kidneys. There is an abnormal and excessive production of a fiber-like protein called collagen in the skin or internal organs.

Spondyloarthropathies—a group of rheumatic diseases principally affecting the spine. One common form—ankylosing spondylitis—may also affect the hips, shoulders, and knees as the tendons and ligaments around the bones and joints become inflamed, resulting in pain and stiffness. Another form—reactive arthritis or Reiter's syndrome—develops after an infection involving the lower urinary tract, bowel, or other

organ and is commonly associated with eye problems, skin rashes, and mouth sores.

Gout—results from deposits of needle-like crystals of uric acid in the joints. The crystals cause inflammation, swelling, and pain in the affected joint, which is often the big toe.

Infectious arthritis—caused by infectious agents, such as bacteria or viruses. Parvovirus arthritis and gonococcal arthritis are examples of infectious arthritis. Arthritis symptoms may also occur in Lyme disease, which is caused by a bacterial infection following the bite of certain ticks.

Psoriatic arthritis—occurs in some patients with psoriasis, a scaling skin disorder. This form often affects the joints at the ends of the fingers and toes and is accompanied by changes in the fingernails and toenails. Back pain may occur if the spine is involved.

Bursitis—involves inflammation of the bursae, small, fluid-filled sacs that help reduce friction between bones and other moving structures in the joints. The inflammation may result from arthritis in the joint or injury or infection of the bursae. Bursitis produces pain and tenderness and may limit the movement of nearby joints. ■

Radiofrequency Identification Technology:

Protecting the Drug Supply

The FDA has stepped up its efforts to improve the safety and security of the nation's drug supply by encouraging use of a state-of-the-art technology that tags product packaging electronically. The technology, called radiofrequency identification, or RFID, allows manufacturers and distributors to more precisely track drug products through the supply chain.

RFID makes it easier to ensure that drugs are authentic, and it also creates an electronic pedigree—a record of the chain of custody from the point of manufacture to the point of dispensing. Electronic pedigrees will improve patient safety and protect the public health by allowing wholesalers and retailers to rapidly identify, quarantine, and report suspected counterfeit drugs and conduct efficient, targeted recalls.

In November 2004, the FDA published a compliance policy guide for industry on implementing RFID studies and pilot programs. Acting FDA Commissioner Dr. Lester M. Crawford says the agency's actions were designed with one main goal: "to increase the safety of medications consumers receive by creating the capacity to track a drug from the manufacturer all the way to the pharmacy."

The FDA acknowledged the leadership of Johnson & Johnson in establishing standards for RFID technology and participating in RFID pilot studies. The agency also applauded initiatives announced by Pfizer, GlaxoSmith-Kline, and Purdue Pharma.

Pfizer announced its plans to place RFID tags on all bottles of Viagra (sildenafil) intended for sale in the United States in 2005. GlaxoSmith-Kline has announced that it intends to begin using RFID tags on at least one product deemed susceptible to counterfeiting.

Purdue Pharma announced that it is placing RFID tags on bottles of the pain reliever OxyContin (oxycodone) to make it easier to authenticate, as well as to track and trace the medication. OxyContin, which is a controlled substance, has been subject to abuse, theft, and diversion. Based on the availability of sufficient RFID tags, Purdue also plans to tag bottles of Palladone (hydromorphone), a newly approved product to treat persistent moderate-to-severe pain.

The FDA considers electronic pedigrees to be a type of "electronic safety net," which allows illicit drug transactions to be rapidly identified and potentially transmitted to the FDA. This could improve the agency's ability to conduct investigations of suspected counterfeiting or the diversion of prescription drugs.



Purdue Pharma L.P.

Radiofrequency identification tags can be read only with a special scanner held within inches of the label.

The FDA believes its compliance guide will clear the way for more pilot programs that involve RFID tagging of all packages of certain products, especially those that are highly likely to be counterfeited. The FDA hopes that more firms will use RFID technology and gain experience with transferring, storing, and securing data that RFID provides.

The scope of the compliance guide is based on information the FDA obtained concerning RFID feasibility studies examining the use of this technology for various business purposes, including inventory control and tracking and tracing of drugs. To encourage these studies, the guide announces the FDA's intention to exercise enforcement discretion if certain studies trigger regulatory requirements.

The FDA's actions are key steps in implementing a major recommendation of the agency's report, "Combating Counterfeit Drugs." That report recommended that RFID technology be in widespread use throughout the pharmaceutical industry by 2007. ■

Take the FDA Consumer QUIZ

What age group is most likely to be affected by multiple sclerosis? How should you respond if you think someone is having a stroke? What's "capsule endoscopy"? Does getting a sunburn increase your risk for skin cancer? To test your knowledge of these and other health-related topics, take our quiz.

Hint: The answers to all of these questions can be found in the March-April 2005 issue of FDA Consumer (and at the bottom of this page). Good Luck!



1. At what age is multiple sclerosis most frequently diagnosed?

- a. during the teen-age years
- b. between 10 and 12
- c. between 60 and 70
- d. between 20 and 50
- e. 80 and over

2. Studies have shown that people with multiple sclerosis who exercise:

- a. often have relapses triggered by exercise
- b. have more fatigue
- c. have less fatigue
- d. have improved cardiovascular health
- e. c and d

3. How many people in the United States are diagnosed with multiple sclerosis every week?

- a. between 50 and 100
- b. about 200
- c. about 300
- d. more than 500

4. How many Americans' everyday activities are limited because of arthritis?

- a. 80,000
- b. 8 million
- c. 750,000
- d. 2.5 million

5. Osteoarthritis can affect:

- a. hands and spine
- b. weight-bearing joints such as knees and hips
- c. both men and women
- d. all of the above

6. Approximately how many people in the United States have a stroke each year?

- a. 100,000
- b. 300,000
- c. 450,000
- d. 700,000

7. What should you do if you think you are having a stroke?

- a. call your family doctor to schedule an appointment
- b. call 911 immediately for emergency help
- c. wait to see if the symptoms go away
- d. lie down and try to get some sleep

8. About how many people who recover from a stroke will have another within five years?

- a. 5 percent
- b. 10 percent
- c. 15 percent
- d. 25 percent

9. How many sunburns increase a person's risk for skin cancer?

- a. three
- b. two
- c. one
- d. sunburn is not related to the risk for skin cancer

10. Capsule endoscopy involves:

- a. having a doctor insert a long, slender medical instrument down the throat
- b. having a doctor insert a long tube into the colon to view the interior
- c. having a person swallow a miniature camera that takes pictures inside the body
- d. performing a medical procedure inside a compression chamber where a patient can breathe better

Answers

1.d, 2.e, 3.b, 4.b, 5.d, 6.d, 7.b, 8.d, 9.c, 10.c

By John Henkel

How to Figure Your Body Mass Index

The latest government figures show that more than 60 percent of U.S. adults are overweight or obese. Carrying this extra weight puts them at a greater risk of developing heart disease, stroke, some cancers, diabetes, or other diseases. But just what is meant by "overweight" or "obese"?

A reliable indicator is body mass index, or BMI. It's a number that gauges total body fat, allowing male and female adults to determine if they are underweight, normal weight, overweight, or obese. You can calculate this number by dividing your weight by your height squared. An easier way, however, is to use the handy BMI calculator the National Heart, Lung, and Blood Institute has created at www.nhlbisupport.com/bmi/bmicalc.htm. With it, you can see where you stand in the body fat spectrum and establish if you have a risk factor that should be addressed.

One caveat: Though BMI can be a strong predictor of serious disorders, it does have limitations in that it may overestimate body fat in those with a muscular build and underestimate it in older persons who have lost muscle mass. For this reason, it's always best to discuss your BMI with a health care professional.

Note that the calculator is just for figuring adult BMIs. Arriving at this number for children and teens is a bit trickier. That's because children's bodies change as they grow. Also, boys and girls differ in their body fatness as they mature. On a special site that shows how to determine a child's BMI, the Centers for Disease Control and Prevention explains that BMI decreases during the preschool years, then increases into adulthood. This "BMI-for-age" site is at www.cdc.gov/nccddp/dnpa/bmi/bmi-for-age.htm.

Learning More About Autism

For many of us, exposure to information about the neurological disorder autism is likely limited to the movie "Rain Man." But autism actually is fairly common, affecting as many as 1 in 500 children, according to the National Institute of Child Health and Human Development (NICHD). Often diagnosed by age 3, autism is about four times as likely to affect boys as it is girls. Autism-related behaviors can range in impact from mild to disabling. In most cases, no underlying cause can be identified, but researchers are investigating the possible role of infectious, metabolic, genetic, and environmental factors.

Want to learn more about autism? Three federal Web sites have a wealth of material:

- The NICHD's *Facts About Autism* site offers a useful overview of the disorder, with an easy-to-understand explana-

tion of current theories about what causes autism. The site is located at www.nichd.nih.gov/publications/pubs/autism1.htm.

- The National Institute of Neurological Disorders and Stroke's "Autism Fact Sheet" also gives a very readable summary, with sections on the role of inheritance, current autism treatments, and research into the disorder. Go to www.ninds.nih.gov/disorders/autism/detail_autism.htm.

- The Centers for Disease Control and Prevention's *Autism Information Center* explains that autism affects people in different ways. These "autism spectrum disorders" cover varying degrees of problems with social skills, speech and language, and repeated behaviors or routines. The CDC's site also has a rundown of states that are sponsoring autism research and other programs. Go to www.cdc.gov/ncbddd/dd/ddautism.htm.

FDA and the Emerging Nanotechnology Field

In the very near future, we'll be surrounded by products created through nanotechnology. Already this science—defined as research and development on a scale smaller than a living cell—is being used to create novel materials for applications in electronics, biomedical, pharmaceutical, cosmetics, and other industries. Products derived from nanotechnology, such as new paints, dental bonding agents, burn and wound dressings, and sunscreens are on the market now.

Because some of these products, as well as others that are proposed, fall within the FDA's oversight, the agency has created a Web site to help clarify nanotechnology regulation. At www.fda.gov/nanotechnology, the agency explains that some of these new products fall neatly into the categories of drugs, devices, or other areas within FDA purview. Others, such as a drug delivery device, are considered "combination products" requiring a special kind of oversight.

The Web site contains several slide presentations and links to other resources, including www.nano.gov, which offers a good overview of government activities in nanotechnology. ■

John Henkel is a member of the FDA's Website Management Staff.

Increasing Stroke Awareness

By Jim Baranski



A few months ago, I overheard an interesting conversation on a flight from Los Angeles to New York. Two businessmen were sitting across the aisle from me deep in conversation when I heard the word "stroke."

One of the men asked, "Did you hear that John had a stroke last week?" The other responded, "You're kidding ... where?" I anticipated that the answer would be "at the office"

or "at home." But instead I heard him say, "I'm not sure, I think in his arm, maybe his heart. I don't know."

This reminded me a little of myself before I became involved with the dreaded disease called a stroke, and I decided to share my story with them. Before my involvement with the National Stroke Association (NSA) a little over three years ago, the word stroke first made me think of time on the golf course with clients. Or, I thought it was a condition that affected grandparents. I didn't know that stroke was synonymous with a "brain attack." I had heard about chest pain and heart attacks, lumps and cancer, but nothing about sudden headaches and brain attacks.

What I have since learned is frightening. More women die of stroke than breast cancer. Stroke is the third leading cause of death in the United States behind cancer and heart disease. And with at least 700,000 strokes occurring annually, it is a leading cause of disability.

I have met with numerous stroke survivors and their caregivers from all over the country. I have seen stroke's impact first hand, and it does not discriminate. Gender, age, race, income, profession, you name it ... stroke knows no boundaries. Few survivors are left with identical deficits. Because stroke is a brain attack, there is no telling where or how much of one's brain will die. With every tick of the clock, brain cells are lost. Hence the phrase "time is brain."

Many of these stroke survivors have shared with me the challenges of recovery and rehabilitation. The frustration of being able to comprehend when spoken to, but unable to speak. To barely walk, but never run. To eat, but not taste. To lose all dignity. To be a burden to family and friends.

Some stroke survivors suffer memory loss. They may need a reminder to help them finish a sentence or remember what to do next. They may be confused and have behavior changes. They may have difficulty controlling emotional

responses, which might mean sudden laughing or crying for no apparent reason. Having a stroke can also cause depression, and a depressed person may refuse or neglect to take medication or may not be motivated to perform exercises that improve mobility. Stroke survivors may also experience pain. The weight of a paralyzed arm can cause pain in the shoulder, or pain can be traced to nerve damage. And lying or sitting in one position too long can cause the body and joints to stiffen and ache.

Now, for the good news. Many strokes are preventable. Hypertension, cholesterol, diabetes, obesity, and smoking are known risk factors for stroke and can be managed with behavior modification and modern therapeutics.

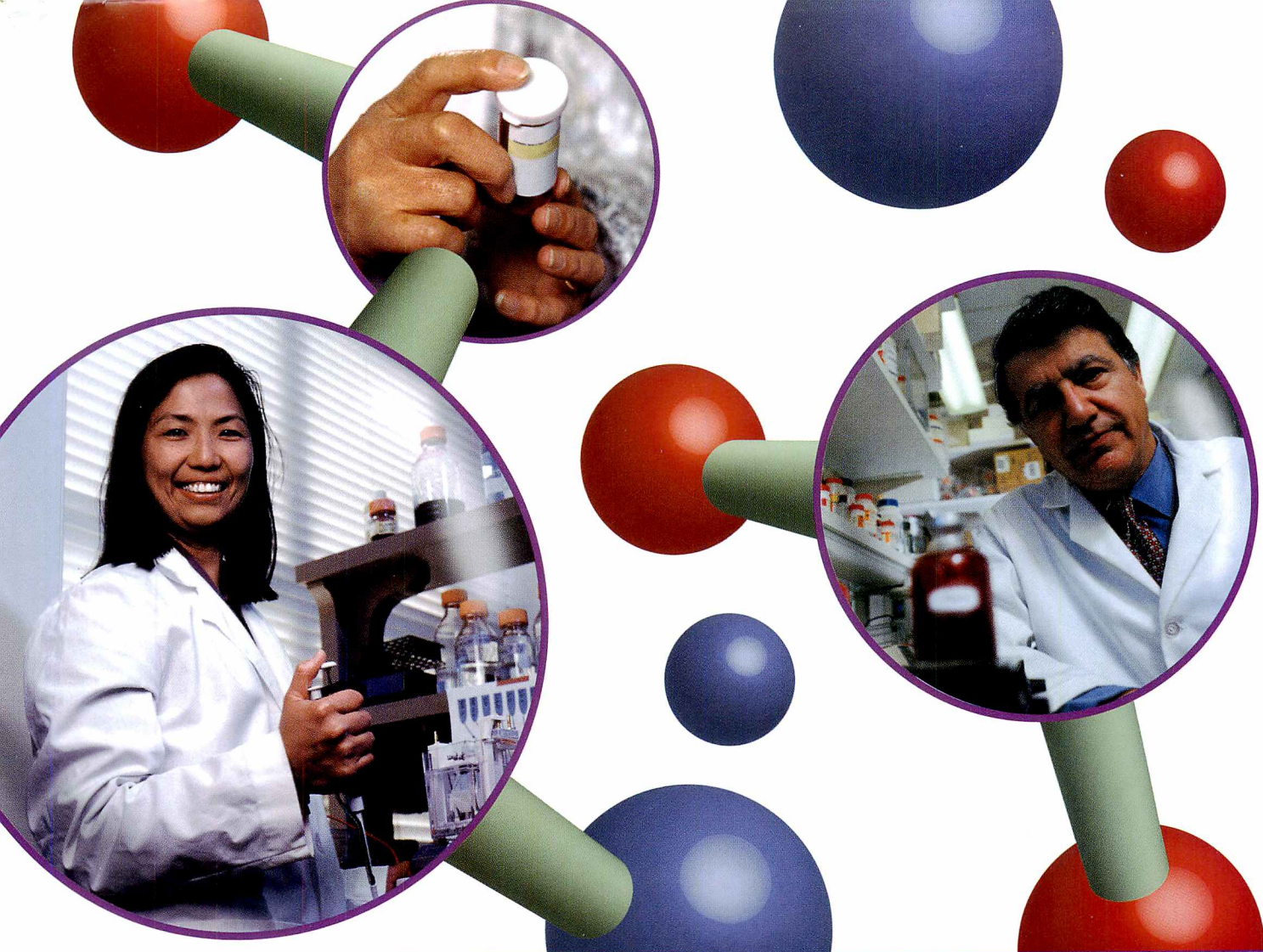
Advances in the acute treatment of stroke and the development of stroke centers in hospitals across the country are providing patient care never before available. Research in recovery and rehabilitation for stroke survivors is suggesting that the brain may be able to "rewire" itself, compensating for cell damage.

What do you need to know in order to take advantage of these advancements for yourself or a loved one? Know the symptoms. The key to the symptoms is that they occur suddenly, with little or no warning. Sudden headache, vision and speech impairment, dizziness, and numbness of face or limbs are all symptoms of a stroke. If you think you or a loved one is having a stroke, call 911 immediately.

Finally, as the plane pulled up to the gate and I concluded my mini-stroke seminar with the businessmen, one of them asked, "How do I know how I measure up to the risk factors for stroke?" I encouraged him to talk with his doctor. This is always a good idea if you have a health concern. Oh yeah, John, their co-worker, was 42 years old.

At NSA, we work to create greater awareness that stroke doesn't only happen to older people. We are aggressively taking steps to reduce the incidence and impact of stroke for all people, young and old. ■

Jim Baranski is chief executive officer and executive director of the National Stroke Association.



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